STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 158531

TO: Kevin Weddington **Location: rem/3A65/3C70** **Art Unit: 1614** **August 3, 2005** **Case Serial Number: 10/615282**	**From: P. Sheppard** **Location: Remsen Building** **Phone: (571) 272-2529** **sheppard@uspto.gov**

Search Notes

KEM- SCIC

Access DB# 158531

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Y. Weddington Examiner #: 68082 Date: 7-7-05
Art Unit: 1614 Phone Number 30 272-0587 Serial Number: 10/615,282
Mail Box and Bldg/Room Location: 3A65 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEY

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

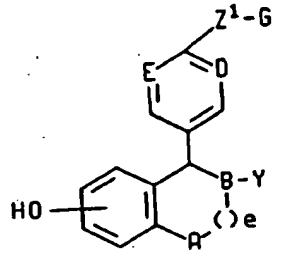
Title of Invention: _____

Inventors (please provide full names): David B. MacLean; ~~David B. MacLean~~
David D. Thompson

-54-

CLAIMS

1. A method of inhibiting a pathological condition which is susc ptible or partially susceptible to inhibition by an estrogen, antiestrogen or estrogen agonist, which comprises administering to a mammal in need of inhibition of said pathological condition selected from the group consisting of uterine cancer, adjuvant breast cancer, breast disorders, male breast cancer, migraine, incontinence, vaginal atrophy, bladder infection, senile gynecomastia, diabetes, hyperglycemia, failure of wound healing, melanoma, impotence, inflammatory bowel disease, CNS and GI disorders caused by an excess of tackykinins, decreased libido, immune system disorders, decreased fertility, pulmonary hypertensive disease, acne, seborrhea, autoimmune disease, Turner's syndrome, alopecia, hirsutism, disorders related to an excess of neurokinin and obsessive-compulsive disorders including smoking and alcohol abuse, an effectiv amount of a compound of formula I



I

wherein:

A is selected from CH_2 and NR;

B, D and E are independently selected from CH and N;

Y is

(a) phenyl, optionally substituted with 1-3 substituents independently selected from R^4;

(b) naphthyl, optionally substituted with 1-3 substituents independently selected from R^4;

(c) C_3-C_8 cycloalkyl, optionally substituted with 1-2 substituents independently selected from R^4;

...ituted with 1-2 substituents

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=> d his ful

     (FILE 'HOME' ENTERED AT 11:28:03 ON 03 AUG 2005)

     FILE 'REGISTRY' ENTERED AT 11:29:15 ON 03 AUG 2005
L19           21 SEA SSS SAM L14 OR L16 AND L7
L20         9814 SEA SSS FUL L14 OR L16 AND L7
L21              STR
L22              STR
L23           87 SEA SUB=L20 SSS FUL L22

     FILE 'HCAPLUS' ENTERED AT 11:39:59 ON 03 AUG 2005
L24          130 SEA ABB=ON  PLU=ON  L23
L25           33 SEA ABB=ON  PLU=ON  L24(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR
                 ?PHARM?)
                 D STAT QUE
                 D IBIB ABS HITSTR L25 1-33
L26           58 SEA ABB=ON  PLU=ON  L24 AND (CARDIOVASCULAR DISEASE?/CV OR
                 ATHEROSCLEROSIS?/CV OR HYPOGONADISM?/CV OR HYPERPLASIA?/CV OR
                 OSTEOPOROSIS?/CV OR LIBIDO?/CV)
L27           15 SEA ABB=ON  PLU=ON  L24(L) (HEART(W)DISEASE OR ?ATHEROSCL? OR
                 ?HYPOGONAD? OR ?HYPERPLA? OR ?OSTEOPOR? OR ?LIBID?)
L28           37 SEA ABB=ON  PLU=ON  (L26 OR L27) NOT L25
                 D STAT QUE L28
                 D IBIB ABS HITSTR L28 1-37
L29           60 SEA ABB=ON  PLU=ON  L24 NOT (L25 OR L28)
L30            8 SEA ABB=ON  PLU=ON  L29 AND PD=<FEBRUARY 28, 1996
                 D STAT QUE L30
                 D IBIB ABS HITSTR L30 1-8


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:    2 AUG 2005  HIGHEST RN 857941-82-3
     DICTIONARY FILE UPDATES:   2 AUG 2005  HIGHEST RN 857941-82-3

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
     ************************************************************

     Structure search iteration limits have been increased.  See HELP SLIMITS
     for details.
```

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE HCAPLUS

FILE COVERS 1907 - 3 Aug 2005 VOL 143 ISS 6
FILE LAST UPDATED: 2 Aug 2005 (20050802/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:39:59 ON 03 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 3 Aug 2005 VOL 143 ISS 6
FILE LAST UPDATED: 2 Aug 2005 (20050802/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d stat que
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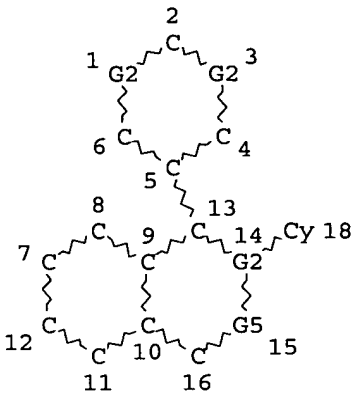
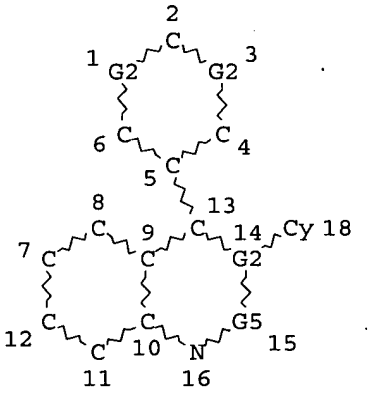
L14 STR



VAR G2=C/N
REP G5=(0-2) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

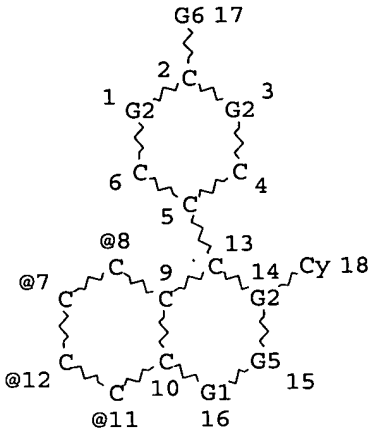
STEREO ATTRIBUTES: NONE
L16 STR



VAR G2=C/N
REP G5=(0-2) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L20 9814 SEA FILE=REGISTRY SSS FUL L14 OR L16 AND L7
L22 STR



N~G3 @19 20

C~G4~CH3 @21 22 23

O~C @24 25

S~C @26 27

OH @28

VAR G1=CH2/NH/19
VAR G2=CH/N
VAR G3=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/21
REP G4=(3-4) C
REP G5=(0-2) C
VAR G6=CH2/24/26
VPA 28-7/8/11/12 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L23 87 SEA FILE=REGISTRY SUB=L20 SSS FUL L22
L24 130 SEA FILE=HCAPLUS ABB=ON PLU=ON L23
L25 33 SEA FILE=HCAPLUS ABB=ON PLU=ON L24(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARM?)

=>
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=> d ibib abs hitstr l25 1-33

L25 ANSWER 1 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:490384 HCAPLUS
DOCUMENT NUMBER: 143:42681
TITLE: Anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer
INVENTOR(S): Wang, Yan; Pachter, Jonathan A.; Bishop, Walter R.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

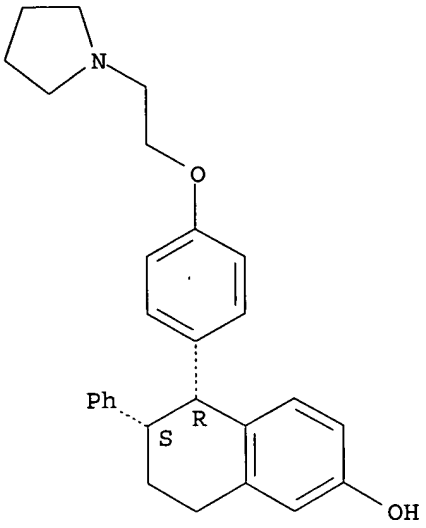
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005052005	A1	20050609	WO 2004-US38842	20041119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005136063	A1	20050623	US 2004-993395	20041119
PRIORITY APPLN. INFO.:			US 2003-524732P	P 20031121

AB The present invention provides combinations including a binding composition, such as an anti-IGFR1 antibody, in association with a chemotherapeutic agent. The antibody is e.g. a human monoclonal antibody recognizing human IGFR-1, especially soluble IGFR-1. The chemotherapeutic agent is selected from a taxane, topoisomerase inhibitor, signal transduction inhibitor, cell cycle inhibitor, farnesyl protein transferase inhibitor, EGFR inhibitor, HER2 inhibitor, VEGFR inhibitor, MAP kinase inhibitor, MEK kinase inhibitor, AKT kinase inhibitor, mTOR inhibitor, etc. Methods for using the combinations to treat medical conditions, such as cancer, are also provided.

IT **180916-16-9**, Lasofoxifene
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-IGFR-1 antibodies in combination with **chemotherapeutic** agent for treating cancer)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:283340 HCAPLUS
DOCUMENT NUMBER: 142:341912
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and an estrogen agonist/antagonist
INVENTOR(S): Lee, Andrew George
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027924	A1	20050331	WO 2004-IB2900	20040906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005070512	A1	20050331	US 2004-943568	20040916

PRIORITY APPLN. INFO.: US 2003-504521P P 20030919

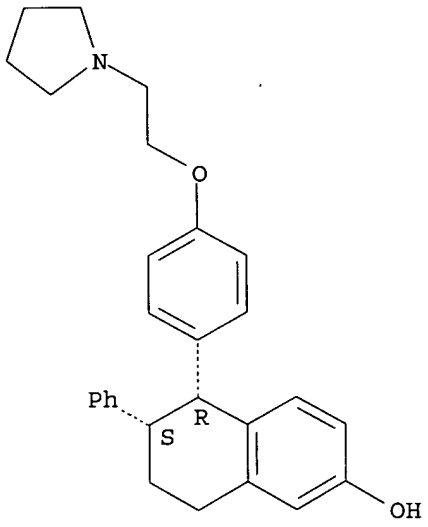
AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an estrogen agonist/antagonist or a pharmaceutically acceptable salt or prodrug

thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-Ia,25-dihydroxyvitamin D3 and (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol, or a pharmaceutically acceptable salt or prodrug thereof.

IT **180916-16-9P 848439-14-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**pharmaceutical** combinations of 2-alkylidene-19-nor-vitamin D derivs. and an estrogen agonist/antagonist)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

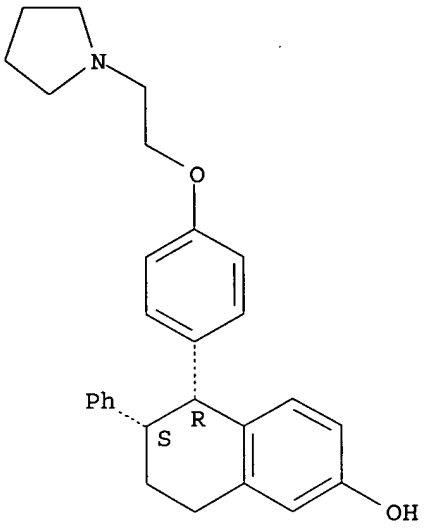


RN 848439-14-5 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

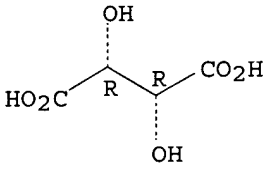
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:259887 HCAPLUS
DOCUMENT NUMBER: 142:336518
TITLE: Preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivatives as androgen receptor modulators
INVENTOR(S): Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025579	A1	20050324	WO 2004-US28641	20040902

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501664P P 20030910
OTHER SOURCE(S): MARPAT 142:336518
GI

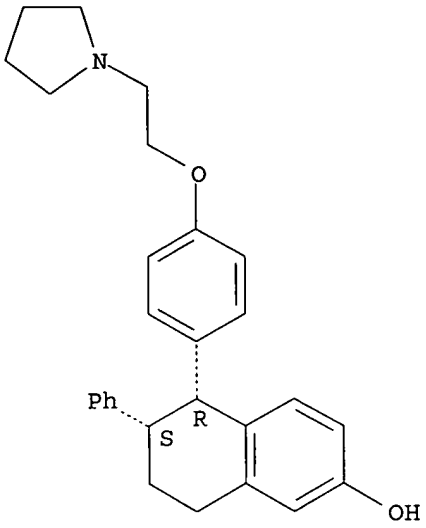
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, provided that at least U, V, W, and D = CH; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-azaandrost-1-ene derivative II was reacted with 2,3-diaminopyridine in presence of silver triflate to give 17β-carboxamide derivative III, which, on heating with polyphosphoric acid, afforded 17β-imidazopyridinyl-3-oxo-4-aza-5α-androst-1-ene derivative IV. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant **therapeutics**; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their **therapeutic** uses)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:259881 HCAPLUS
DOCUMENT NUMBER: 142:336517
TITLE: Preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner
INVENTOR(S): Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025572	A1	20050324	WO 2004-US28655	20040902

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501789P P 20030910
OTHER SOURCE(S): MARPAT 142:336517
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

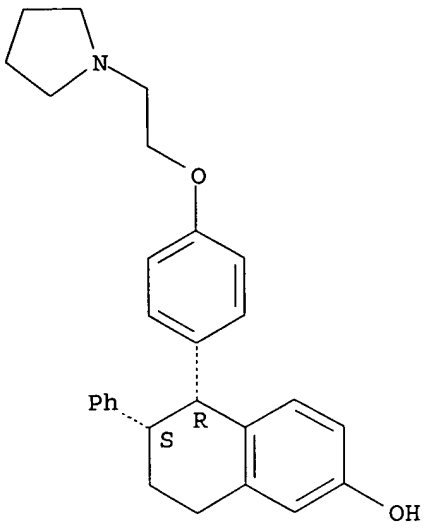
AB 17-Heterocyclic-4-aza-5α-androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH) was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5α-androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant **therapeutics**; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their **therapeutic** uses)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



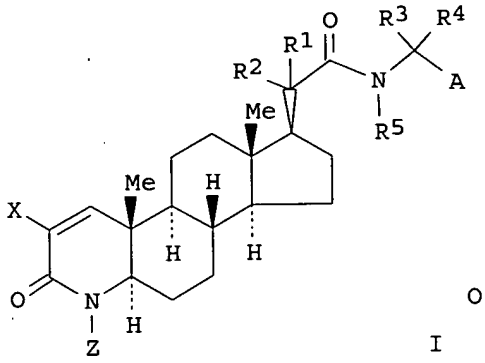
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:58320 HCAPLUS
DOCUMENT NUMBER: 142:156210
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005606	A2	20050120	WO 2004-US20539	20040625
WO 2005005606	A3	20050602		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483675P P 20030630
OTHER SOURCE(S): MARPAT 142:156210
GI



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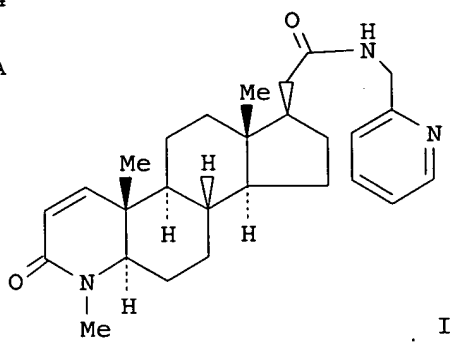


II

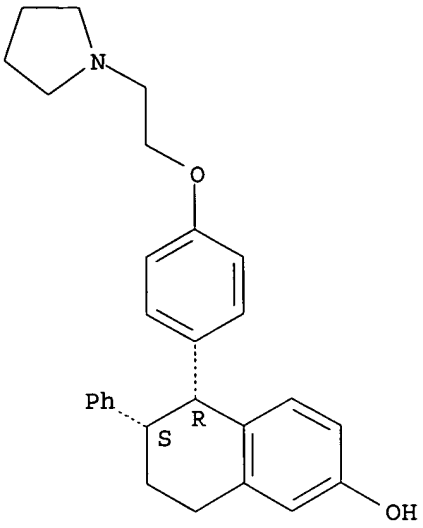
AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; Z = H, CF3, carbonylalkyl, alkyl, alkoxy, halo, CH2OH; A = aromatic ring having 0-4 heteroatoms; polycyclic ring system having one or more aromatic rings and 0-4 heteroatoms; R1, R2, R3, R4, R5 = H, halo, alkyl, amino, alkylamino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino, etc.; R1R2, R3R4 = oxo, spirocycloalkyl], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 2-aminomethylpyridine. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, benign prostatic hyperplasia (BPH), cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant **therapeutics**; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their **therapeutic** uses)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

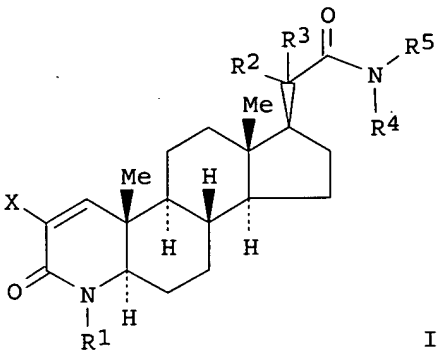


L25 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:55196 HCAPLUS
DOCUMENT NUMBER: 142:156209
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005380	A2	20050120	WO 2004-US20548	20040625
WO 2005005380	A3	20050602		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483784P P 20030630
OTHER SOURCE(S): MARPAT 142:156209
GI



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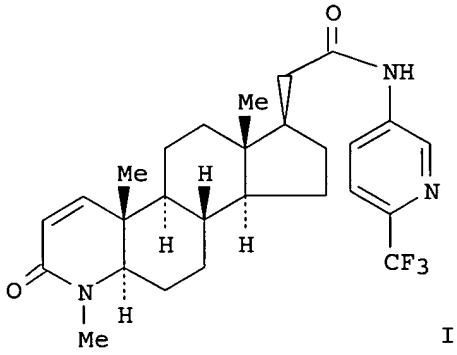


II

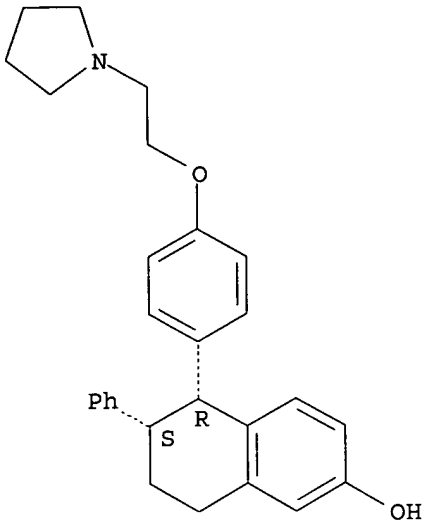
AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; R1 = H, CF3, alkyl, alkoxy, halo, amino, alkylamino, CH2OH; R2, R3 = H, halo, alkyl, amino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino; R2R3 = oxo, spirocycloalkyl; R4, R5 = H, halo, alkyl, alkenyl, alkynyl, carbonylalkyl, carbonylalkenyl, cabonylalkynyl, cycloalkyl, heterocyclyl, cycloheteroalkyl, carboxyaryl, etc.], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 3-amino-6-trifluoromethylpyridine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive impairment, decreased libido, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their **therapeutic** uses)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



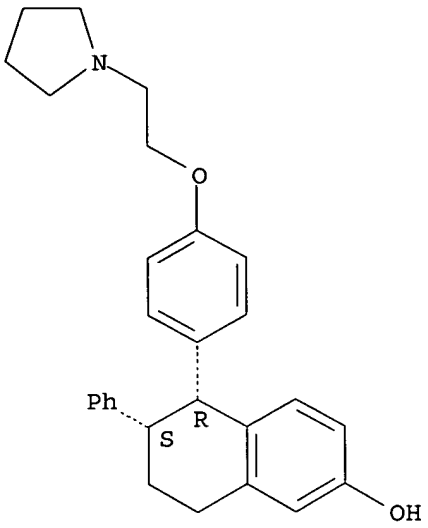
L25 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:43403 HCAPLUS
DOCUMENT NUMBER: 142:290471
TITLE: New osteoporosis drugs under development
AUTHOR(S): Itabashi, Akira
CORPORATE SOURCE: Department of Clinical Laboratory Medicine, Saitama Medical School, Saitama, 350-0492, Japan
SOURCE: Naibunpi, Tonyobyoka (2004), 19(3), 247-255
CODEN: NATOFF; ISSN: 1341-3724
PUBLISHER: Kagaku Hyoronsha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. New osteoporosis drugs under development is reviewed including the role of bisphosphonate formulation, selective estrogen receptor modulator (SERM) such as LY353381, lasofoxifene and bazedoxifene, parathyroid hormone, strontium ranelate, and anti-RANKL antibody in the treatment of osteoporosis.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new osteoporosis **drugs** under development)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

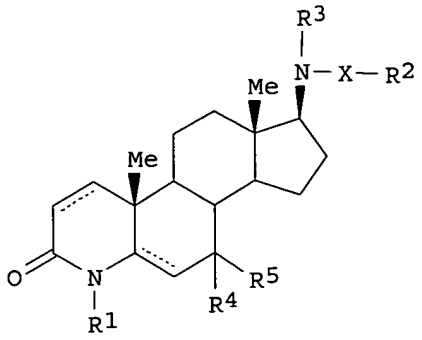


L25 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1015853 HCAPLUS
DOCUMENT NUMBER: 142:1359
TITLE: Identification and synthesis of androgen receptor modulators and therapeutic uses thereof
INVENTOR(S): Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100874	A2	20041125	WO 2004-US13787	20040503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-468579P P 20030507
OTHER SOURCE(S): MARPAT 142:1359
GI



I

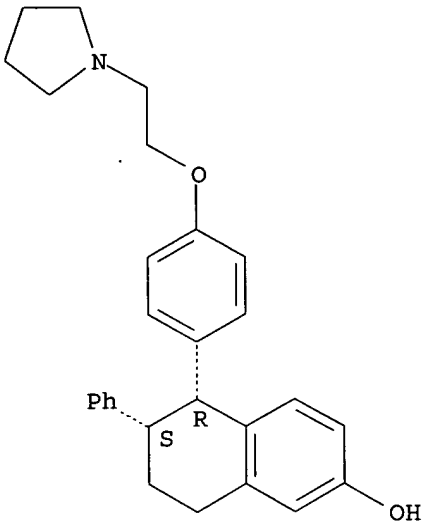
AB Compds. of structural formula (I) as herein defined are disclosed as useful in a method for modulating the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of agonizing the androgen receptor in a patient, and in particular the method wherein the androgen receptor is antagonized in the prostate of a male patient or in the uterus of a female patient and agonized in bone and/or muscle tissue. Method for the synthesis of those compds., as well as techniques for the screening of androgen receptor modulation capacity of those compds. are exemplified. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including: osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, post-menopausal symptoms in women, female sexual dysfunction, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, arthritis and joint repair, alone or in combination with other active agents. In addition, these compds. are useful as pharmaceutical composition ingredients alone and in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and **therapeutic** uses thereof)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965090 HCAPLUS
DOCUMENT NUMBER: 141:389284
TITLE: Methods and compositions using gonadotropin hormone releasing hormone
INVENTOR(S): Porchet, Herve; Heimgartner, Frederic; Curdy, Catherine; Ducrey, Bertrand
PATENT ASSIGNEE(S): Debiopharm S.A., Switz.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096259	A1	20041111	WO 2004-IB1334	20040430

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2003-IB1680 A 20030430

AB The present invention relates to compns. comprising two sustained release formulations, the first being capable of releasing a gonadotropin releasing hormone composition and the second an estrogenic composition The compns. of the invention can be employed for an improved androgen deprivation therapy of prostate cancer, in which therapy loss of bone mineral d. and the occurrence and severity of hot flashes are minimized through the

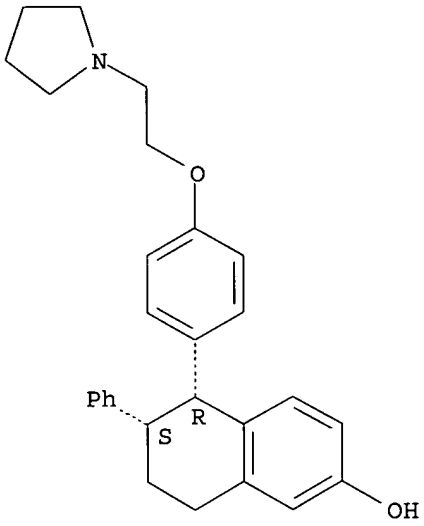
maintenance of a minimally adequate estrogen level.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(gonadotropin hormone-releasing hormone formulations for improved androgen deprivation in prostate cancer **therapy**)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:759835 HCAPLUS

DOCUMENT NUMBER: 141:277616

TITLE: Preparation of 3-(1-[3-(1,3-benzothiazol-6-yl)propylcarbamoyl]cycloalkyl)propanoic acid derivatives as nep inhibitors

INVENTOR(S): Hepworth, David

PATENT ASSIGNEE(S): Pfizer Inc., UK

SOURCE: U.S. Pat. Appl. Publ., 27 pp., which
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180941	A1	20040916	US 2004-800065	20040312
WO 2004080985	A1	20040923	WO 2004-IB822	20040309

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

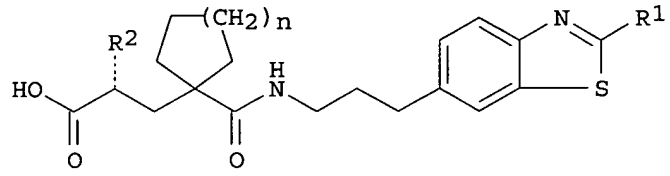
NL 1025709	A1	20040916	NL 2004-1025709	20040312
NL 1025709	C2	20050314		

PRIORITY APPLN. INFO.:

GB 2003-5916	A	20030314
US 2003-464608P	P	20030422
GB 2003-29143	A	20031216
US 2004-538079P	P	20040120

OTHER SOURCE(S): MARPAT 141:277616

GI



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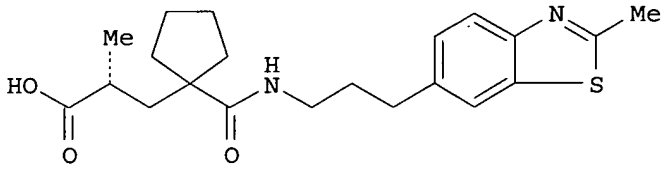


II

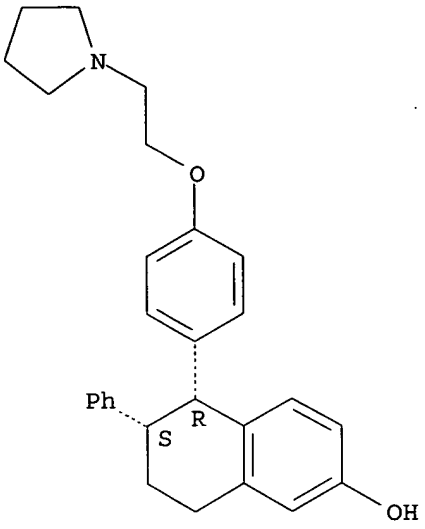
AB The invention relates to the use of title compds. I [R1 = H or Me; R2 = Me or Et; n = 1 or 2] as inhibitors of neutral endopeptidase enzyme (NEP), processes for the preparation thereof, intermediates used in the preparation thereof and compns. containing said inhibitors. Thus, e.g., II was prepared by amidation of 1-[(2R)-3-tert-butoxy-2-methyl-3-oxopropyl]cyclopentane carboxylic acid with 3-(2-methyl-1,3-benzothiazol-6-yl)propylamine dihydrochloride (preparation given) with subsequent hydrolysis to provide the free acid. I have been demonstrated to possess IC50 values of <20 nanomolar in tests for NEP inhibition and demonstrate a selectivity over soluble secreted endopeptidase (SEP) of at least 1000 fold. These inhibitors have utility in a variety of therapeutic areas including the treatment of male and female sexual dysfunction, particularly female sexual dysfunction (FSD), especially wherein the FSD is female sexual arousal disorder (FSAD).

IT **180916-16-9**, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**codrug**; preparation of ([(benzothiazolyl)propylcarbamoyl]cycloalkyl)propanoic acid derivs. as inhibitors of neutral endopeptidase enzyme)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



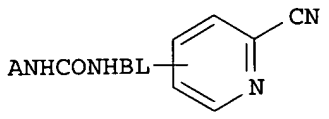
L25 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:756710 HCAPLUS
DOCUMENT NUMBER: 141:277628
TITLE: Preparation of ureidophenoxycyanopyridines as anticancer drugs.
INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen; Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma, Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei; Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu, Qingming
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078747	A1	20040916	WO 2004-US6286	20040301
WO 2004078747	C1	20041104		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235829	A1	20041125	US 2004-788029	20040227
US 2004229937	A1	20041118	US 2004-789446	20040301
US 2005032798	A1	20050210	US 2004-788405	20040301
US 2005038031	A1	20050217	US 2004-788426	20040301

PRIORITY APPLN. INFO.: US 2003-450323P P 20030228
US 2003-450324P P 20030228
US 2003-450348P P 20030228

OTHER SOURCE(S): MARPAT 141:277628

GI



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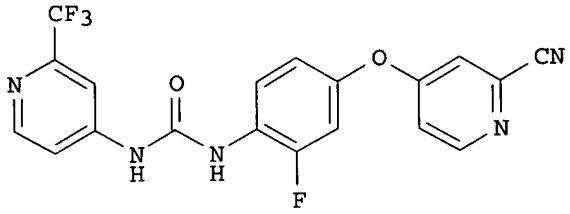


II

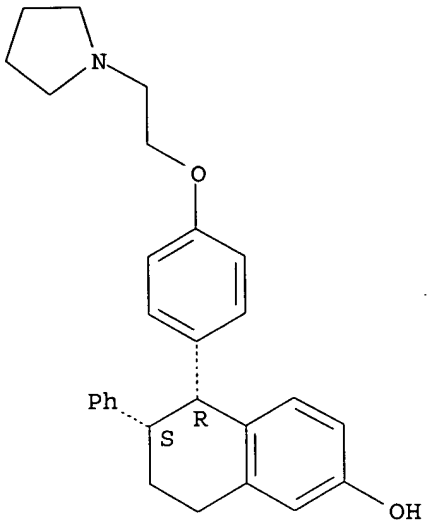
AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxy], were prepared Thus, 2-trifluoromethyl-4-pyridylamine was stirred 20 h with carbonyldiimidazole in CH2Cl2; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC50 = 7.86 nM to >1600 nM.

IT **180916-16-9**, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer **drugs**)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

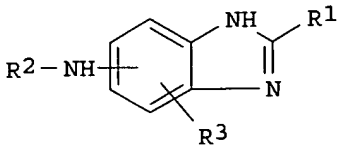


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:412812 HCAPLUS
DOCUMENT NUMBER: 140:406808
TITLE: Preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators
INVENTOR(S): Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara; Duggan, Mark E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004041277	A1	20040521	WO 2003-US34345		20031028
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2504044	AA	20040521	CA 2003-2504044		20031028
PRIORITY APPLN. INFO.:			US 2002-422914P	P	20021101
			WO 2003-US34345	W	20031028

OTHER SOURCE(S): MARPAT 140:406808
GI



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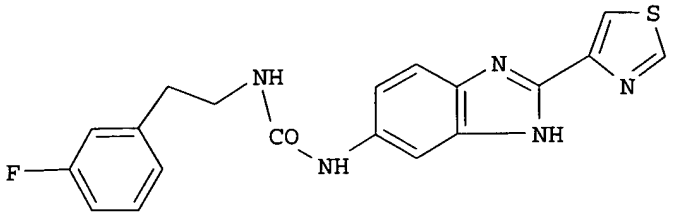


II

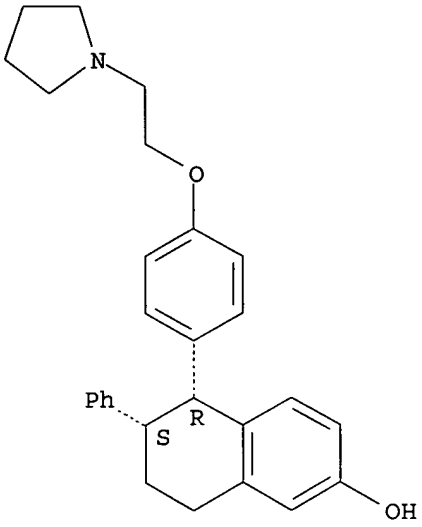
AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, HIV-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents. Although the methods of preparation are not claimed, 6 example prepns. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 = -(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen, -(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl, -S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

IT **180916-16-9**, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**codrug**; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:2847 HCAPLUS
DOCUMENT NUMBER: 140:71530
TITLE: Use of cyclothiocarbamate derivatives as selective androgen antagonists in contraception, hormone replacement therapy and in treatment of other hormone-related conditions
INVENTOR(S): Fensome, Andrew; Grubb, Gary; Harrison, Diane Deborah; Winneker, Richard Craig; Zhang, Puwen; Kern, Jeffrey Curtis; Terefenko, Eugene Anthony
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000801	A2	20031231	WO 2003-US19751	20030623
WO 2004000801	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2489847	AA	20031231	CA 2003-2489847	20030623
US 2004006060	A1	20040108	US 2003-601481	20030623
BR 2003012024	A	20050322	BR 2003-12024	20030623
EP 1515725	A2	20050323	EP 2003-761263	20030623

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2002-391871P P 20020625
WO 2003-US19751 W 20030623
OTHER SOURCE(S): MARPAT 140:71530
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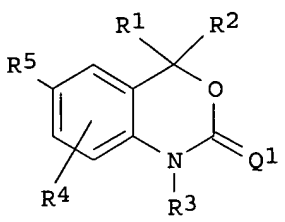

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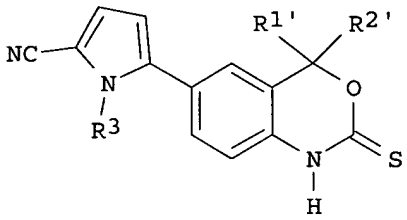
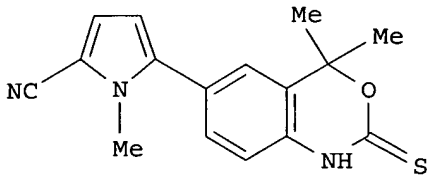


II



III

AB The present invention provides methods of inducing contraception which includes delivering to a female a composition containing cyclothiocarbamates (shown as I and II; variables defined below; e.g. III) or tautomers thereof, in a regimen which involves delivering ≥1 of a selective estrogen receptor modulator. Methods of providing hormone replacement therapy and for treating carcinomas, dysfunctional bleeding, uterine leiomyomata, endometriosis, and polycystic ovary syndrome is provided which includes delivering I or II and a selective estrogen receptor modulator are also described. III (5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile) showed significant antagonistic activity towards androgens in L929 cells over a nine point dose response (IC50 = 109 nM) and only marginal agonistic activity at the maximum concentration tested (i.e., 10 nM). Although neither I nor II nor the methods of preparation are claimed, 6 example prepns. are included. For example, 1-methyl-5-[2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6-yl]-1H-pyrrole-2-carbonitrile was prepared in 5 steps (32, 58, 52, 79, and 49 % yields, resp.) starting from phenylcarbamic acid tert-Bu ester, cyclobutanone and tBuLi in Et2O and involving intermediates tert-Bu [2-(1-hydroxycyclobutyl)phenyl]carbamate, spiro[3,1-benzoxazine-4,1'-cyclobutan]-2(1H)-one, 6-bromospiro[3,1-benzoxazine-4,1'-cyclobutan]-2(1H)-one, and 1-methyl-5-[2-oxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6-yl]-1H-pyrrole-2-carbonitrile. For I: R1 and R2 = H, (un)substituted C1 to C6 alkyl, (un)substituted C2-C6 alkenyl, (un)substituted C2-C6 alkynyl, (un)substituted C3-C8 cycloalkyl, (un)substituted aryl, (un)substituted C-based heterocyclic ring having in its backbone 1-3 heteroatoms, CORA, and NRBCORA; or R1 and R2 are fused to form a ring (a), (b) and (c), wherein said ring is (un)substituted by 1-3 substituents H and C1 to C3 alkyl ((a) a C-based 3 to 8 membered saturated spirocyclic ring; (b) a C-based 3 to 8 membered spirocyclic ring having ≥1 C-C double bonds; and (c) a 3 to 8 membered spirocyclic ring having in its backbone 1-3 heteroatoms O, S and N). R3 = H, OH, NH2, (un)substituted C1 to C6 alkyl, (un)substituted C3-C6 alkenyl, (un)substituted alkynyl, and CORC; R4 = H, halogen, CN, NO2,

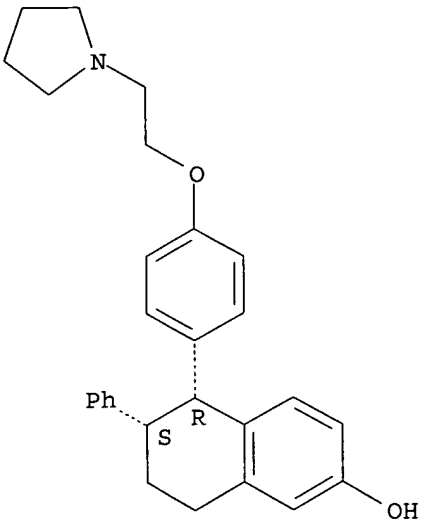
(un)substituted C1 to C6 alkyl, C1 to C6 alkoxy, C1 to C6 aminoalkyl; R5 = an X/Y/Z-substituted Ph or a five or six membered C-based heterocyclic ring having in its backbone 1-3 heteroatoms O, S, SO, SO2, and NR6 and having one or two independent substituents H, halogen, CN, NO2, (un)substituted C1 to C4 alkyl, (un)substituted C1 to C3 alkoxy, (un)substituted C1 to C3 aminoalkyl, (un)substituted C1 to C3 perfluoroalkyl, (un)substituted 5 or 6 membered C-based heterocyclic ring having in its backbone 1-3 heteroatoms, (un)substituted C1 to C3 thioalkyl, CORF, and NRGCORF; Q1 = S, NR7, and CR8R9; addnl. details are given in the claims. For II: R1' = Me, Et, trifluoromethyl; R2' = Me, Et, trifluoromethyl; or R1' and R2' are joined to form a spirocyclic ring containing 3 to 7 C atoms; and R3 =C1 to C4 alkyl; other variables are as for I.

IT **180916-16-9**, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulator as **codrug**; use of cyclothiocarbamate derivs. as selective androgen antagonists in contraception, hormone replacement **therapy** and in treatment of other hormone-related conditions)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

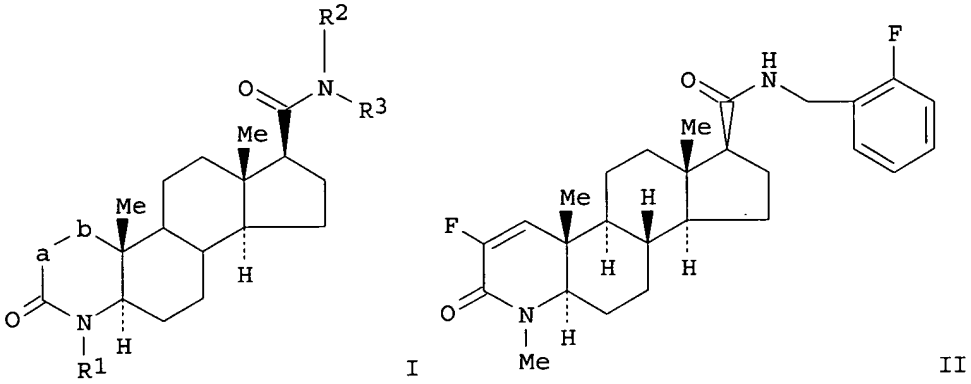
ACCESSION NUMBER:	2003:757525 HCAPLUS
DOCUMENT NUMBER:	139:277056
TITLE:	Preparation of fluorinated 4-aza-androstan-3-one-17β-carboxamide derivatives as androgen receptor modulators
INVENTOR(S):	Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S):	Merck & Co., Inc., USA
SOURCE:	PCT Int. Appl., 95 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003077919	A1	20030925	WO 2003-US8277		20030307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2478186	AA	20030925	CA 2003-2478186		20030307
EP 1485095	A1	20041215	EP 2003-714228		20030307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK					
BR 2003008355	A	20050125	BR 2003-8355		20030307
US 2005165039	A1	20050728	US 2003-507239		20030307
PRIORITY APPLN. INFO.:			US 2002-363822P	P	20020313
			WO 2003-US8277	W	20030307

OTHER SOURCE(S): MARPAT 139:277056

GI



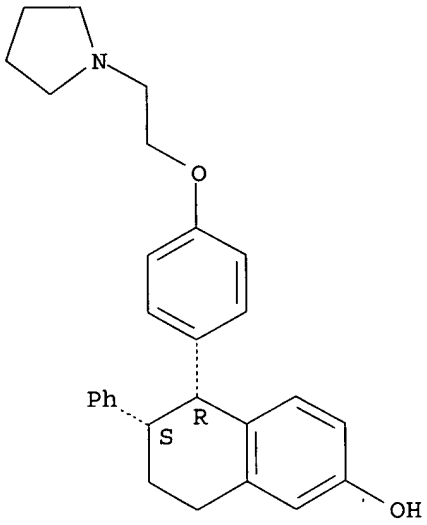
AB Fluorinated 4-aza-androstan-3-one-17β-carboxamide derivs., such as I [a-b = CF:CH, CHFCH2, CF2CH2; R1 = H, CH2OH, (un)substituted alkyl; R2 = H, alkyl; R3 = alkyl, cycloheteroalkyl, aryl, heteroaryl; R2R3 = 5 or 6-membered ring fused with a 5- or 6-membered aromatic ring system having 0-2 heteroatoms], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-aza-androstan-3-one-17β-carboxamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-4-aza-androstan-3-one-17-carboxylic acid Me ester and 2-fluoro-benzylamine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone

reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, cancer cachexia, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant **therapeutics**; preparation of fluorinated 4-aza-androstan-3-one-17β-carboxamide derivs. as androgen receptor modulators and their **therapeutic** uses)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:154278 HCAPLUS
DOCUMENT NUMBER: 138:198670
TITLE: GnRh agonist combination drugs
INVENTOR(S): Furuya, Shuichi; Kusaka, Masami
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015820	A1	20030227	WO 2002-JP8130	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

CA 2458452	AA	20030227	CA 2002-2458452	20020808
JP 2003137814	A2	20030514	JP 2002-231922	20020808
EP 1424080	A1	20040602	EP 2002-758814	20020808

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:	JP 2001-244616	A 20010810
	WO 2002-JP8130	W 20020808

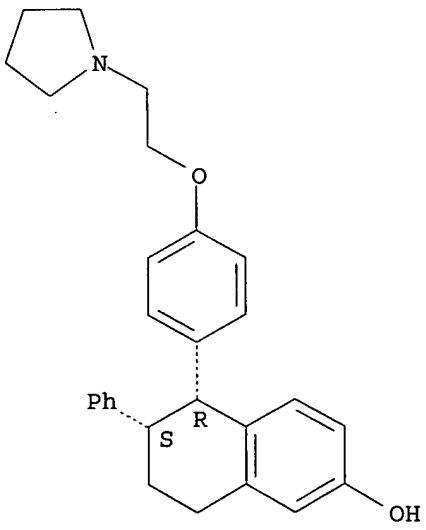
AB In the field of pharmaceuticals, it is intended to provide drugs whereby the preventive and therapeutic effects of a GnRH agonist on various diseases can be enhanced and QOL can be improved. More specifically, combination drugs characterized in that the GnRH agonist is combined with a chemical selected from among SERM, SARM, sex hormone synthesis inhibitors, receptor-type tyrosine kinase inhibitors, bone metabolism regulators, drugs for immunotherapy, cytokine/chemokine inhibitors and endothelin receptor antagonists. Owing to these combinations, excellent effects of enhancing the preventive and therapeutic effects of the GnRH agonist on various diseases and relieving side effects can be established. Furthermore, QOL can be improved thereby.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH agonist combination **drugs** for treating various diseases and relieving side effects)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849406 HCAPLUS
DOCUMENT NUMBER: 137:342136
TITLE: Method for manufacturing a low dose pharmaceutical composition having uniform drug distribution and potency using silicon dioxide
INVENTOR(S): Gierer, Daniel Scott
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002087546	A2	20021107	WO 2002-IB766		20020313
WO 2002087546	A3	20030213			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2445519	AA	20021107	CA 2002-2445519		20020313
EP 1383482	A2	20040128	EP 2002-702671		20020313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EE 200300537	A	20040415	EE 2003-537		20020313
BR 2002009283	A	20040713	BR 2002-9283		20020313
CN 1531423	A	20040922	CN 2002-809255		20020313
JP 2004531537	T2	20041014	JP 2002-584892		20020313
NZ 528886	A	20050429	NZ 2002-528886		20020313
US 2003004182	A1	20030102	US 2002-131556		20020423
ZA 2003007819	A	20041007	ZA 2003-7819		20031007
NO 2003004709	A	20031031	NO 2003-4709		20031021
PRIORITY APPLN. INFO.:			US 2001-287841P	P	20010501
			WO 2002-IB766	W	20020313

OTHER SOURCE(S): MARPAT 137:342136

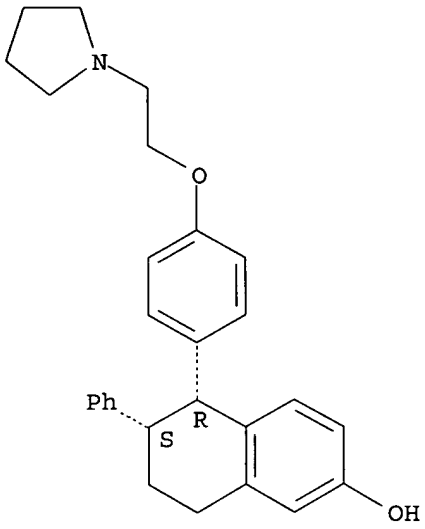
AB A method for manufacturing a pharmaceutical composition having uniform drug distribution and potency is described which utilizes silicon dioxide to reduce the loss of active ingredient, e.g. an estrogen receptor modulator, during the manufacturing process. The method is particularly useful for the manufacture of low dosage tablet compns. For example, lasofoxifene tablets were prepared by compression of dry granulation containing lactose 1052.25 g, microcryst. cellulose 375.00 g, croscarmellose sodium 45.00 g, silicon dioxide 7.50 g and lasofoxifene 5.25 g.

IT **180916-16-9P**, Lasofoxifene
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manufacturing of low dose composition having uniform **drug** distribution and potency using silicon dioxide)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-

pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

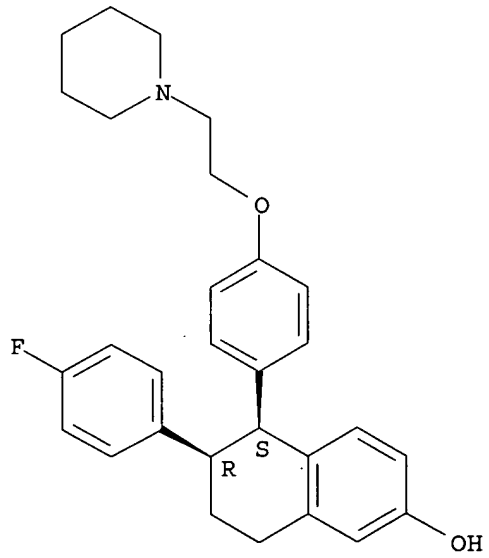
Absolute stereochemistry. Rotation (-).



IT **180915-84-8 180915-86-0 180916-14-7**
180916-15-8 474316-48-8 474316-50-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manufacturing of low dose composition having uniform **drug** distribution and potency using silicon dioxide)

RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

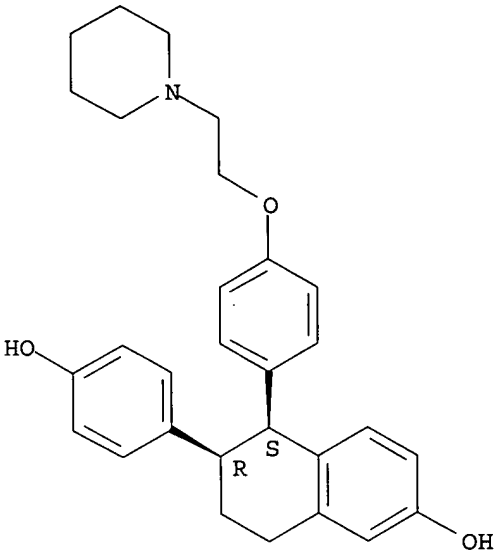
Relative stereochemistry.



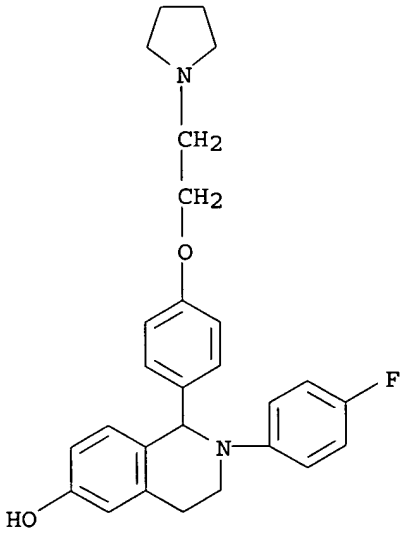
RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-

piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

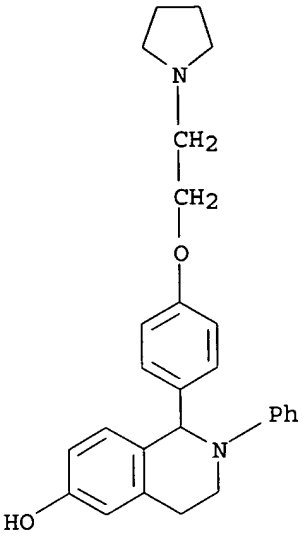
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

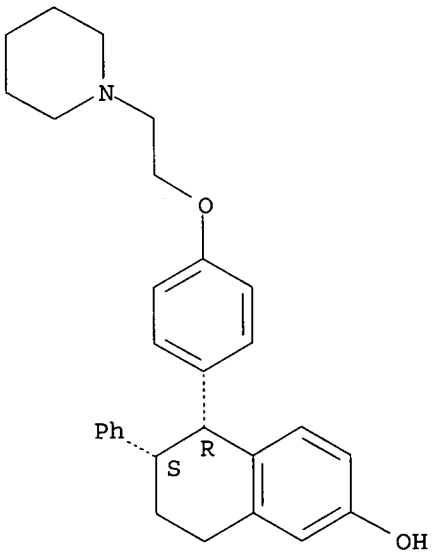


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 474316-48-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown.

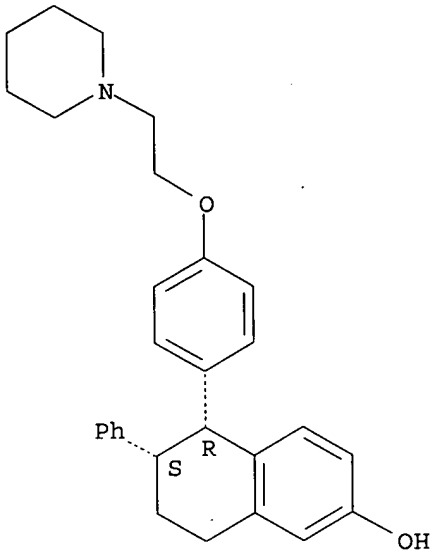


RN 474316-50-2 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 474316-49-9
CMF C29 H33 N O2

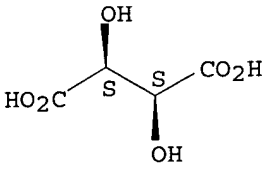
Relative stereochemistry.



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

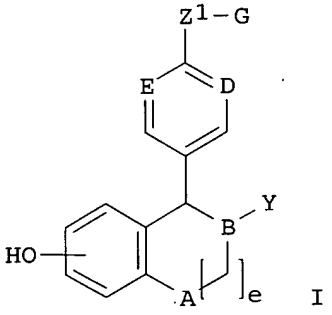


L25 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:426631 HCAPLUS
DOCUMENT NUMBER: 137:16062
TITLE: Combination for treating andropause and related conditions containing estrogen agonists/antagonists and testosterone
INVENTOR(S): McLean, David Burton
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1210951	A2	20020605	EP 2001-309457	20011108
EP 1210951	A3	20030924		

EP 1210951	B1	20050202			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
AT 288303	E	20050215	AT 2001-309457		20011108
ES 2233570	T3	20050616	ES 2001-1309457		20011108
US 2002115676	A1	20020822	US 2001-995130		20011127
CA 2363935	AA	20020530	CA 2001-2363935		20011128
AU 2001095165	A5	20020606	AU 2001-95165		20011129
AU 779964	B2	20050224			
ZA 2001009836	A	20030529	ZA 2001-9836		20011129
NZ 515822	A	20030530	NZ 2001-515822		20011129
JP 2002193809	A2	20020710	JP 2001-365803		20011130
PRIORITY APPLN. INFO.:			US 2000-250071P	P	20001130
OTHER SOURCE(S):	MARPAT 137:16062				

GI



I

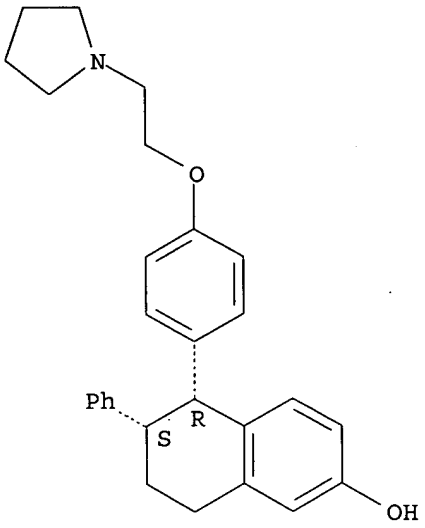
AB The present invention concerns the treatment of andropause and related conditions using a combination of an estrogen agonist/antagonist and testosterone. The Markush structure for the estrogen agonist/antagonist is I, where A = CH2 or NR; B, D, and E = CH or N; Y= a ring; Z1 is linear or part of a ring with G; and G is a linear or a ring. The specifically claimed estrogen agonist/antagonist is (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol or an optical or geometric isomer thereof; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof. Drugs containing the compds. of the invention can be used to treat gynecomastia, lipid disorders, cardiovascular disease, atherosclerosis, hypogonadism, benign prostatic hyperplasia, or osteoporosis; or increasing libido; or maintaining or improving vascular reactivity in a male patient. A treatment kit containing (a) one or more pharmaceutical compns. comprising an estrogen agonist/antagonist and testosterone; and (b) instructions for administering the pharmaceutical composition is also claimed.

IT **180916-16-9D**, isomers, salts, N-oxides, esters, quaternary ammonium salts, or **prodrugs**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination for treating andropause and related conditions containing estrogen agonists/antagonists and testosterone)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:51266 HCAPLUS
DOCUMENT NUMBER: 136:107533
TITLE: Pharmaceutical compositions containing estrogenic agents
INVENTOR(S): Benjamin, Eric Joel; Dulin, Wendy Ann; Suryawanshi, Jiwaji Gulabrao
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003987	A2	20020117	WO 2001-US20993	20010629
WO 2002003987	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2415058	AA	20020117	CA 2001-2415058	20010629
US 2002031548	A1	20020314	US 2001-896226	20010629
EP 1309327	A2	20030514	EP 2001-950781	20010629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012242	A	20030624	BR 2001-12242	20010629
JP 2004502733	T2	20040129	JP 2002-508441	20010629
NO 2003000030	A	20030303	NO 2003-30	20030103
ZA 2003001004	A	20040505	ZA 2003-1004	20030205

PRIORITY APPLN. INFO.: US 2000-216192P P 20000706
WO 2001-US20993 W 20010629

AB This invention comprises novel pharmaceutical carrier or excipient systems and oral pharmaceutical formulations comprising as an active ingredient raloxifene, tamoxifen, droloxifene, arzoxifene, or CP 336156, or analogs, or an indole derivative and the excipients chosen from fillers, glidants, lubricants, wetting agents and antioxidants. Thus, a modified formulation contained micronized TSE-424 acetate 5.00, Lactose NF 41.00, microcryst. cellulose 35.00, pregelatinized starch 10.00, sodium lauryl sulfate 1.50, L-ascorbic acid 1.50, sodium starch glycolate 5.50, Mg stearate 0.50 and water qs to 100%.

IT **190791-29-8**, CP 336156
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** compns. containing estrogenic agents)

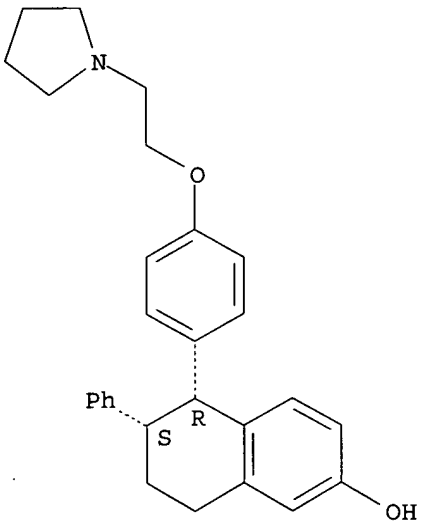
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

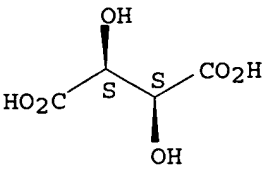
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

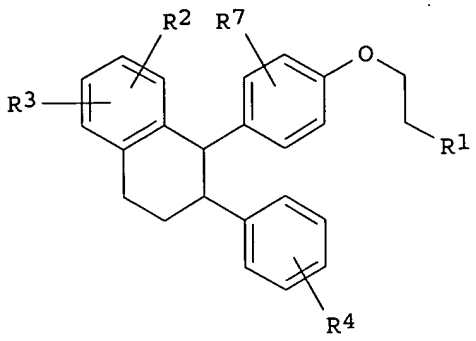
Absolute stereochemistry.



L25 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:762983 HCAPLUS
DOCUMENT NUMBER: 135:303769
TITLE: Preparation of estrogen agonist/antagonist metabolites
INVENTOR(S): Day, Wesley Warren; Johnson, Kim Anne; Prakash, Chandra Aggarwal; Eggler, James Frederick
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001077093	A1	20011018	WO 2001-IB427		20010319
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2405070	AA	20011018	CA 2001-2405070		20010319
EP 1268453	A1	20030102	EP 2001-912069		20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001009838	A	20030121	BR 2001-9838		20010319
NZ 521291	A	20040227	NZ 2001-521291		20010319
JP 2004510693	T2	20040408	JP 2001-575567		20010319
EE 200200580	A	20040615	EE 2002-580		20010319
US 2002042443	A1	20020411	US 2001-825980		20010404
US 6455572	B2	20020924			
BG 107137	A	20030530	BG 2002-107137		20020923
NO 2002004767	A	20021203	NO 2002-4767		20021003
ZA 2002007995	A	20031020	ZA 2002-7995		20021004
PRIORITY APPLN. INFO.:			US 2000-267198P	P	20000407
			WO 2001-IB427	W	20010319

OTHER SOURCE(S): MARPAT 135:303769
GI



I

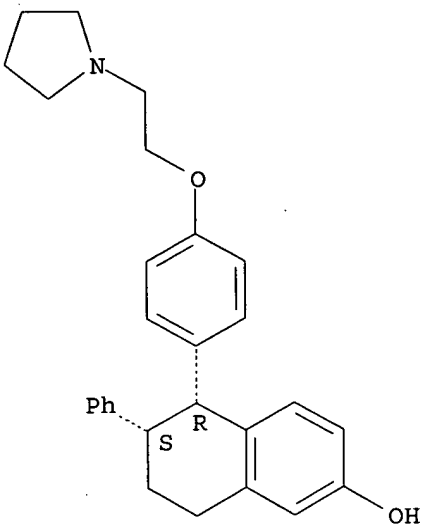
AB This invention relates to compds. represented by formula [I; R1 = pyrrolidin-1-yl, 2-oxopyrrolidin-1-yl, 2-hydroxy-1-pyrrolidin-1-yl, 2-methoxy-1-pyrrolidin-1-yl, NH(CH2)3COR6 (where R6 = OH, NHCH2CO2H); R2, R3, R4, R7 = H, OH, OMe; provided that (a) if R1 is pyrrolidin-1-yl or NH(CH2)3CO2H, and (b) R2 is OH or OMe and R3 and R7 are H, or if R1 is defined in (a) and (c) R2 and R7 are H and R3 is OH or OMe, then R4 is not H] which are mammalian metabolites of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol (PPTN) and are believed to possess significant pharmacol. activities similar or identical to those possessed by the parent PPTN. The compds. of the invention can be used as stds. for anal. assays or as intermediates for the further chemical synthesis or biosynthesis of chemical entities. The invention also relates to pharmaceutical compns. for the treatment of disease and methods of treating disease. Examples of diseases or conditions for which the compds. can be effective include osteoporosis, breast cancer, hyperlipidemia, atherosclerosis, Alzheimer's disease, cataracts, loss of libido, male sexual dysfunction, colon cancer, skin wrinkles, autoimmune disease, alopecia, acne, cardiovascular disease, cataracts, diabetes, endometriosis, female sexual dysfunction, hyperglycemia, obesity, obsessive compulsive disorder, etc. (no data). Thus, 1-[2-[4-(2-Bromo-6,7-dimethoxy-3,4-dihydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine was coupled with phenylboronic acid in the presence of tetrakis(triphenylphosphine)pal ladium and Na2CO3 in EtOH at room temperature for 10 h to give 1-[2-[4-(6,7-dimethoxy-2-phenyl-3,4-dihydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine which was hydrogenated Pd(OH)2 on carbon in a mixture of 2 N aqueous HCl, H2O, and EtOH at 50° under a H atmospheric of 30 psi to give 1-[2-[4-(6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine. The latter compound was heated in a mixture of AcOH and 48% aqueous HBr at 90° for 2 h to give cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2,3-diol and a mixture of cis-3-methoxy-7-phenyl-8-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol and cis-3-methoxy-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol.

IT **180916-16-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(animal metabolism; preparation of metabolites of (-)-cis-phenyl[(pyrrolidinylethoxy)phenyl]tetrahydronaphthalenol estrogen agonist/antagonist as **therapeutic** agents)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

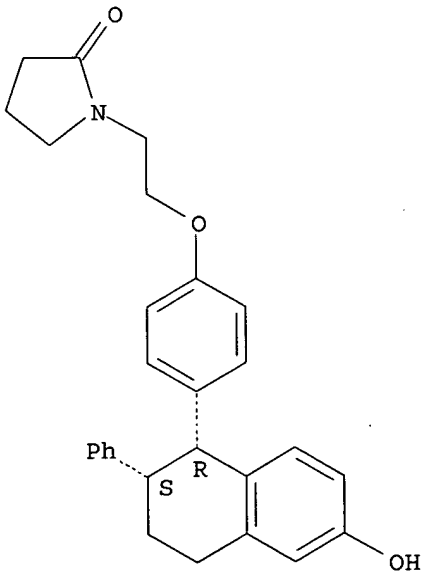


IT **366017-88-1P 366017-89-2P 366470-00-0P**
366470-01-1P 366470-04-4P
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metabolite in mice; preparation of metabolites of (-)-cis-phenyl[(pyrrolidinylethoxy)phenyl]tetrahydronaphthalenol estrogen agonist/antagonist as **therapeutic** agents)

RN 366017-88-1 HCAPLUS

CN 2-Pyrrolidinone, 1-[2-[4-[(1R,2S)-1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl]phenoxy]ethyl]- (9CI) (CA INDEX NAME)

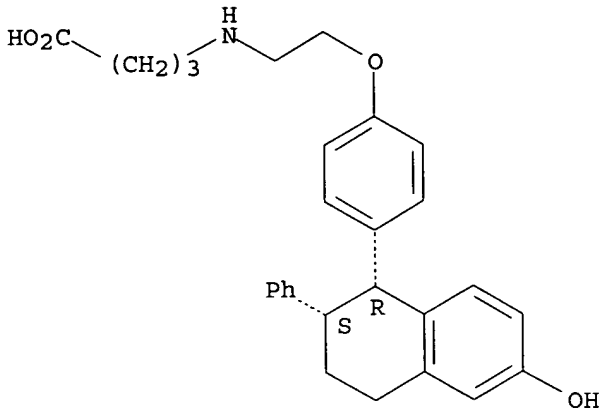
Absolute stereochemistry.



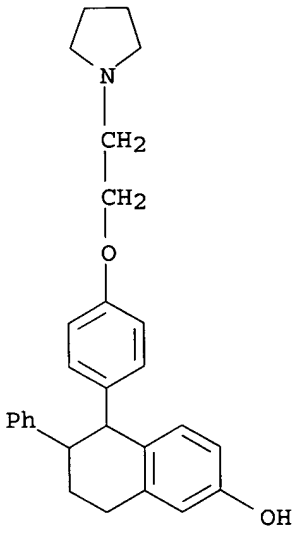
RN 366017-89-2 HCAPLUS

CN Butanoic acid, 4-[[2-[4-[(1R,2S)-1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl]phenoxy]ethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

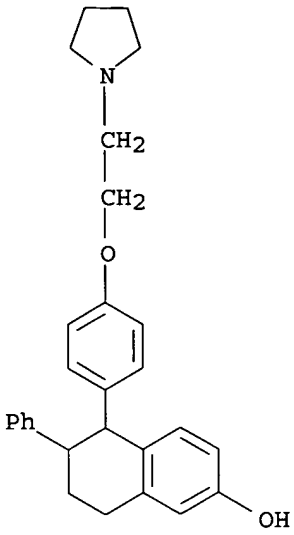


RN 366470-00-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-ar-methoxy-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)



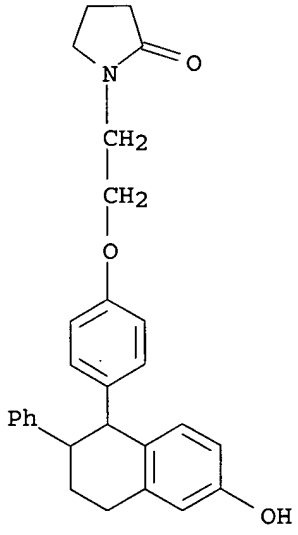
D1—O—Me

RN 366470-01-1 HCAPLUS
CN ar,2-Naphthalenediol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)



D1—OH

RN 366470-04-4 HCAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-[(1R,2S)-1,2,3,4-tetrahydro-ar,6-dihydroxy-2-phenyl-1-naphthalenyl]phenoxy]ethyl]- (9CI) (CA INDEX NAME)

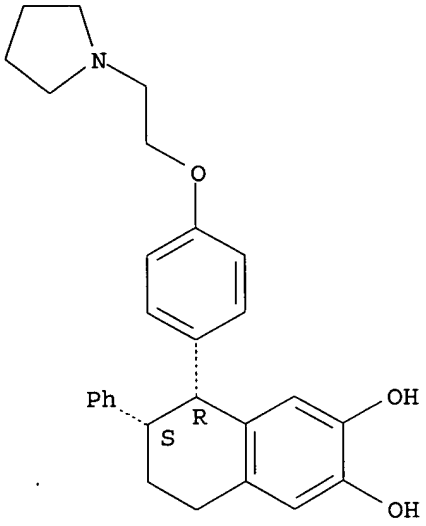


D1—OH

IT **366017-69-8P 366017-70-1P 366017-71-2P**
366017-81-4P 366017-82-5P 366017-83-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of metabolites of (-)-cis-phenyl[(pyrrolidinylethoxy)phenyl]tetrahydronaphthalenol estrogen agonist/antagonist as **therapeutic**

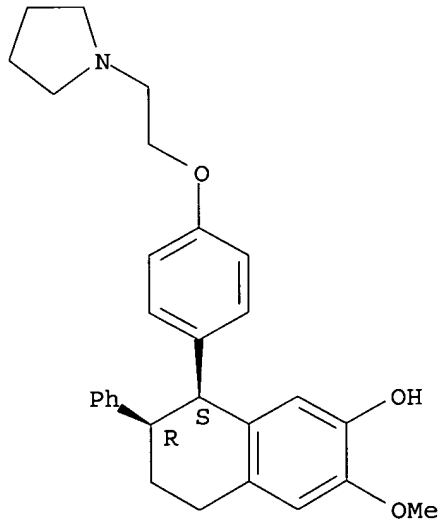
agents)
RN 366017-69-8 HCAPLUS
CN 2,3-Naphthalenediol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



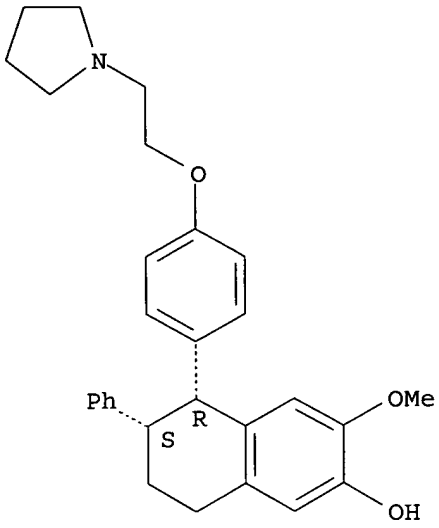
RN 366017-70-1 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-3-methoxy-7-phenyl-8-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (7R,8S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



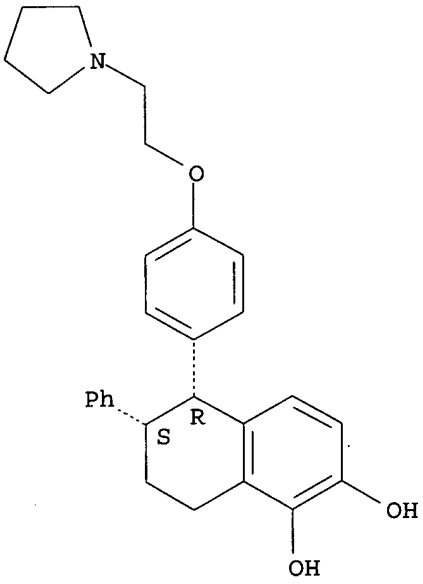
RN 366017-71-2 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-3-methoxy-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



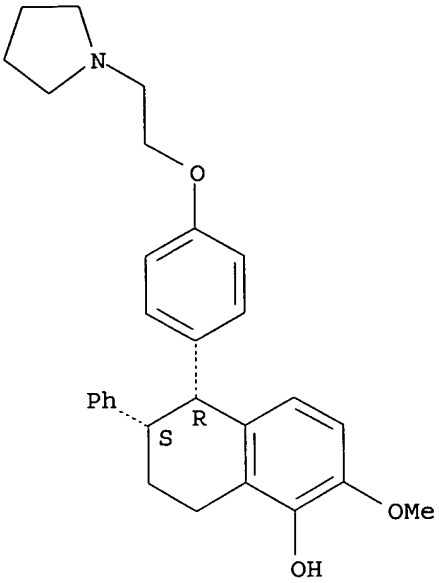
RN 366017-81-4 HCAPLUS
CN 1,2-Naphthalenediol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



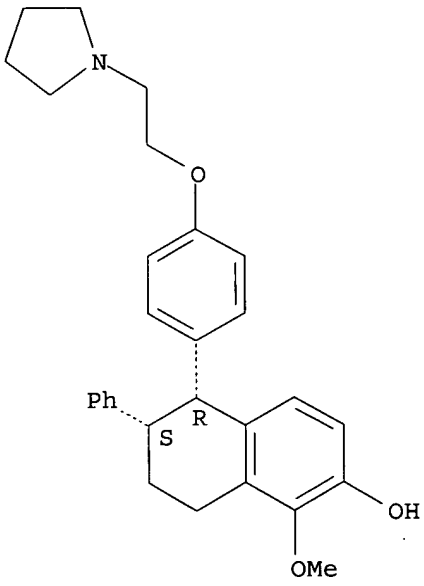
RN 366017-82-5 HCAPLUS
CN 1-Naphthalenol, 5,6,7,8-tetrahydro-2-methoxy-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 366017-83-6 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-1-methoxy-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:704687 HCAPLUS
DOCUMENT NUMBER: 135:262237
TITLE: Ferrous compounds as antioxidants for pharmaceutical

formulations

INVENTOR(S): Wang, Hai
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001261577	A2	20010926	JP 2001-68073	20010312
EP 1145719	A2	20011017	EP 2001-302022	20010306
EP 1145719	A3	20011114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2339705	AA	20010910	CA 2001-2339705	20010308
BR 2001000949	A	20011030	BR 2001-949	20010309
US 2001047034	A1	20011129	US 2001-803455	20010309
US 6423351	B2	20020723		
US 2002183392	A1	20021205	US 2002-155157	20020524
US 6767558	B2	20040727		

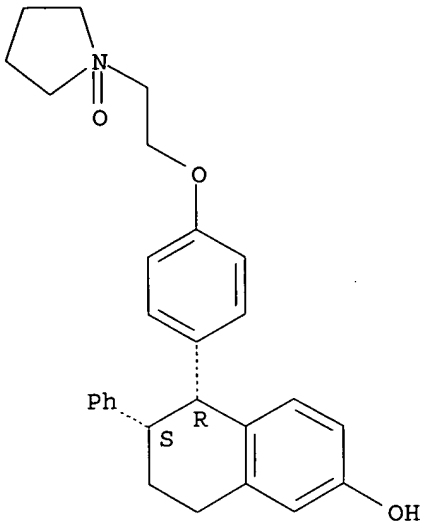
PRIORITY APPLN. INFO.: US 2000-188447P P 20000310
US 2001-803455 A3 20010309

AB This invention relates to the use of Fe(II) compds. to prevent oxidation degradation of easily oxidizable active ingredients in the compns. The easily oxidizable compds. contain ≥ 1 benzyl or amine functional groups. (2S,3S)-N-(5-isopropyl-2-methoxyphenyl)methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]octan-3-amine was mixed with ferrous ammonium sulfate hexahydrate (0.01 %)-containing Avicel, then blended with Mg stearate for tableting. After storage of the tablets at 40° and 75 % relative humidity for 6 wk, negligible amts. of oxidation products were detected by reversed HPLC.

IT **362026-33-3P**
RL: BYP (Byproduct); PREP (Preparation)
(ferrous compds. as antioxidants for **pharmaceutical** formulations)

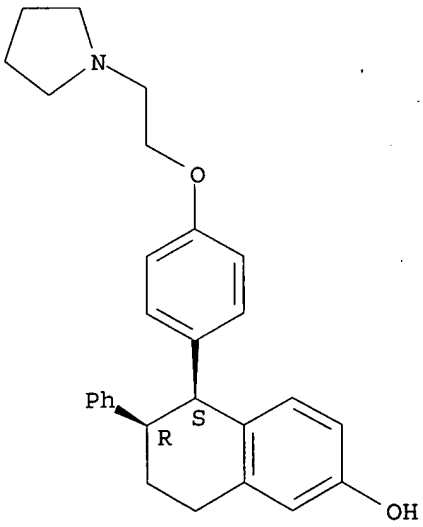
RN 362026-33-3 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-5-[4-[2-(1-oxido-1-pyrrolidinyl)ethoxy]phenyl]-6-phenyl-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **180915-78-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ferrous compds. as antioxidants for **pharmaceutical** formulations)
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L25 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:647817 HCAPLUS
DOCUMENT NUMBER: 135:366221
TITLE: Selective estrogen receptor modulation: the search for an ideal hormonal therapy for breast cancer
AUTHOR(S): Dhingra, Kapil

CORPORATE SOURCE: Hoffmann-La Roche, Inc., Nutley, NJ, 07110, USA
SOURCE: Cancer Investigation (2001), 19(6), 649-659
CODEN: CINVD7; ISSN: 0735-7907
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Female hormones, especially estrogens, play an important role in the pathogenesis of breast neoplasms and are a principal determinant of their biol. behavior. Endocrine manipulation through medical or surgical means can often lead to objective shrinkage of breast tumors. Tamoxifen, a triphenylethylene estrogen receptor modulator, is currently the most widely used hormonal treatment for breast cancer. It has been conclusively demonstrated to reduce the risk of relapse following definitive local therapy (and systemic chemotherapy, when indicated) of invasive or non-invasive breast cancer. Recently, it has also been shown to reduce the incidence of breast cancer in healthy women who are at high risk of developing the disease. In addition, it can prevent osteoporosis and reduce the risk of fractures in postmenopausal women. However, its use is also complicated by an increased incidence of endometrial hyperplasia/carcinoma, venous thromboembolism, cataracts, and in some cases, emergence of tamoxifen-dependent clones of breast cancer. These side effects (except cataracts) are believed to be related to estrogen-agonist effects of tamoxifen. Newer drugs, which are "pure antiestrogens" or inhibitors of estrogen biosynthesis, are devoid of such estrogen-agonist activity and may not have the liability of many of these side effects. However, these agents would also be expected to lack the potentially beneficial effects of tamoxifen on lipids and skeletal system. The ability of tamoxifen to act as an estrogen-agonist or estrogen-antagonist in a tissue-specific fashion has led to the concept of selective estrogen-receptor modulation. Selective estrogen receptor modulators (SERMs), which are devoid of estrogen-agonist effects on the uterus or breast cancer cells but retain potentially beneficial effects on bones and lipids, have been described as "ideal" SERMs. A number of such compds. are currently being tested. Raloxifene is already approved for prevention of osteoporosis and has potential efficacy for prevention and treatment of breast cancer. An analog of raloxifene, LY353381, is currently in Phase II clin. trials for treatment of breast cancer, with promising early results. EM800 and CP336156 are other promising ideal SERMs in clin. trials. These compds. may provide better treatment and chemoprevention alternatives for breast cancer as compared to tamoxifen, aromatase inhibitors, and pure antiestrogens. In addition, they may also prove to be useful for the treatment and prevention of prostate cancer as well as for treating benign gynecol. diseases such as fibroids and endometriosis. Future laboratory efforts should focus on further broadening the efficacy profile of SERMs (e.g., prevention of Alzheimer's disease and elevation of high-d. lipoproteins to improve the likelihood of cardiovascular benefit) and narrowing their side-effect profile (e.g., risk of thromboembolism and hot flashes).

IT **190791-29-8**, CP336156
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulation in hormonal **therapy** for breast cancer in humans)

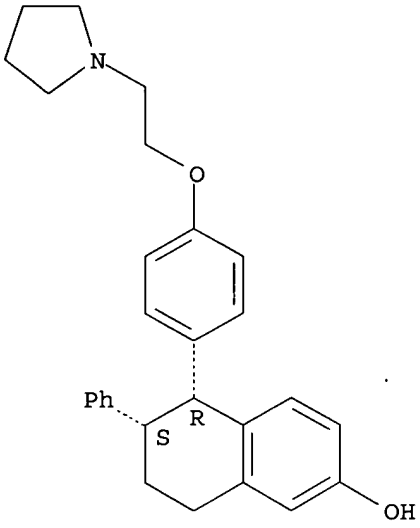
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

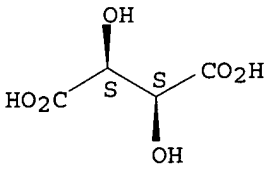
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



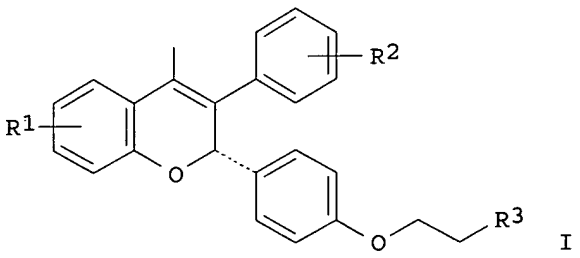
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:564841 HCAPLUS
DOCUMENT NUMBER: 135:132470
TITLE: Selective estrogen receptor modulators in combination with estrogens for therapeutic use
INVENTOR(S): Labrie, Fernand
PATENT ASSIGNEE(S): Endorecherche, Inc., Can.
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054699	A1	20010802	WO 2001-CA86	20010126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395730	AA	20010802	CA 2001-2395730	20010126
EP 1251855	A1	20021030	EP 2001-902194	20010126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008107	A	20030311	BR 2001-8107	20010126
JP 2003520817	T2	20030708	JP 2001-554683	20010126
US 2002198179	A1	20021226	US 2001-52803	20011107
US 2003040510	A1	20030227	US 2001-52824	20011107
US 2003065008	A1	20030403	US 2002-143894	20020509
NO 2002003484	A	20020722	NO 2002-3484	20020722
ZA 2002005926	A	20030724	ZA 2002-5926	20020724
PRIORITY APPLN. INFO.:			US 2000-178601P	P 20000128
			US 2001-771180	A1 20010126
			WO 2001-CA86	W 20010126

OTHER SOURCE(S): MARPAT 135:132470

GI



I

AB Methods for reduction or elimination of the incidence of hot flashes and menopausal symptoms, while decreasing the risk of acquiring breast or endometrial cancer and furthermore treating and/or inhibiting the development of osteoporosis, hypercholesterolemia, hyperlipidemia, atherosclerosis, hypertension, insulin resistance, diabetes, loss of muscle mass, obesity, irregular menstruation, Alzheimer's disease, or vaginal dryness in susceptible warm-blooded animals, including humans, involves administration of selective estrogen receptor modulators, particularly compds. I (R1, R2 = OH, moiety convertible to OH in vivo; R3 = (un)saturated (substituted) pyrrolidinyl, (un)saturated (substituted) piperidinyl, etc.) and an amount of an estrogen or mixed estrogenic/androgenic compound Further administration of bisphosphonates, or a sex steroid precursor is specifically disclosed for the medical treatment and/or inhibition of development of some of these above-mentioned diseases. Pharmaceutical compns. for delivery of active

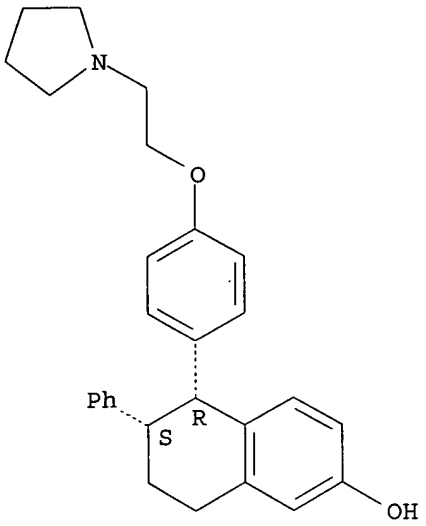
ingredient(s) and kit(s) useful to the invention are also disclosed.

IT **180916-16-9**, Lasofoxifene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulators in combination with estrogens for **therapeutic** use)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:555210 HCAPLUS

DOCUMENT NUMBER: 135:142233

TITLE: Pharmaceutical compositions containing estrogen agonist/antagonist and statins for treatment of osteoporosis and/or for lowering blood cholesterol

INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206845	A2	20010731	JP 2001-15626	20010124
EP 1123717	A2	20010816	EP 2001-300527	20010122
EP 1123717	A3	20031015		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 2003162807	A1	20030828	US 2001-767625		20010123
US 6756401	B2	20040629			
CA 2332214	AA	20010726	CA 2001-2332214		20010124
ZA 2001000675	A	20020724	ZA 2001-675		20010124
AU 2001016675	A5	20010802	AU 2001-16675		20010125
AU 780568	B2	20050407			
NZ 523651	A	20040625	NZ 2001-523651		20010125
US 2004259886	A1	20041223	US 2004-840577		20040506
PRIORITY APPLN. INFO.:			US 2000-188923P	P	20000126
			US 2000-205327P	P	20000421
			US 2000-188293P	P	20000308
			US 2001-767625	A3	20010123

OTHER SOURCE(S): MARPAT 135:142233

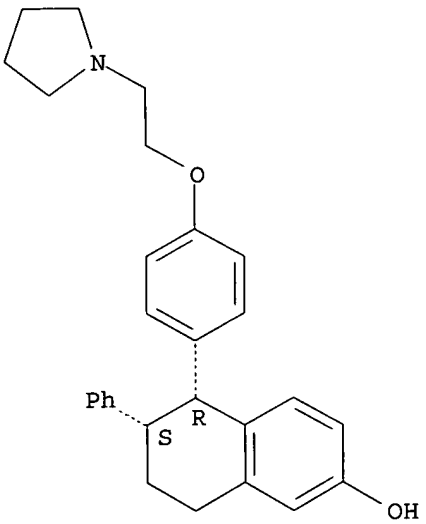
AB The invention provides a composition containing an estrogen agonist/antagonist, and a statin deriv for treatment of osteoporosis and/or for lowering blood cholesterol. The antiosteoporotic effect of (-)-cis-6-phenyl-5-[4-(2-pyrrolidine-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol (PPTN) in ovary-excised rats were examined

IT **180916-16-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** compns. containing estrogen agonist/antagonist and statins for treatment of osteoporosis and/or for lowering blood cholesterol)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **190791-29-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** compns. containing estrogen agonist/antagonist and statins for treatment of osteoporosis and/or for lowering blood cholesterol)

RN 190791-29-8 HCAPLUS

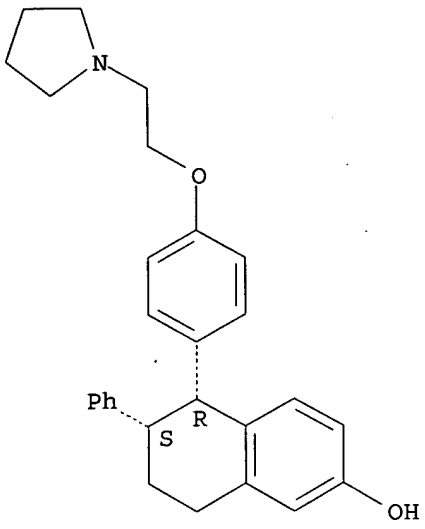
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-

pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

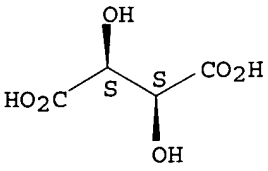
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



L25 ANSWER 24 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:541600 HCAPLUS
DOCUMENT NUMBER: 135:117261
TITLE: Method using estrogen agonists/antagonists for reducing morbidity and the risk of mortality from cardiovascular disease, breast cancer, and osteoporosis
INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1118323	A2	20010725	EP 2001-300159		20010109
EP 1118323	A3	20030521			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CA 2331059	AA	20010712	CA 2001-2331059		20010110
US 2001056099	A1	20011227	US 2001-757817		20010110
ZA 2001000276	A	20020710	ZA 2001-276		20010110
JP 2001226265	A2	20010821	JP 2001-5300		20010112
PRIORITY APPLN. INFO.:			US 2000-175663P	P	20000112

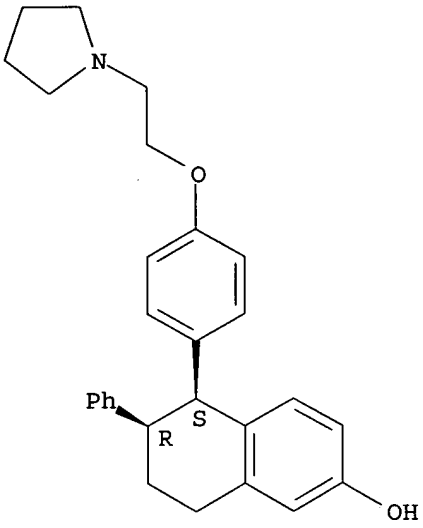
OTHER SOURCE(S): MARPAT 135:117261

AB The invention discloses methods, pharmaceutical compns., and kits useful in reducing cardiovascular morbidity and the risk of mortality in men and post-menopausal women and morbidity and the risk of mortality in post-menopausal women from the combined reduction of breast cancer, osteoporosis and cardiovascular disease by the administration of estrogen agonists/antagonists. The compns. are comprised of an estrogen agonist/antagonist and a pharmaceutically acceptable vehicle, carrier, or diluent. The compns. and methods of treatment are effective while substantially reducing the concomitant liability of adverse effects associated with estrogen administration.

IT **180915-78-0D**, isomers, N-oxides, esters, and **prodrug** derivs. **180915-84-8D**, isomers, N-oxides, esters, and **prodrug** derivs. **180915-86-0D**, isomers, N-oxides, esters, and **prodrug** derivs. **180916-14-7D**, isomers, N-oxides, esters, and **prodrug** derivs. **180916-15-8D**, isomers, N-oxides, esters, and **prodrug** derivs. **180916-16-9D**, isomers, N-oxides, esters, and **prodrug** derivs. **193274-89-4D**, isomers, N-oxides, esters, and **prodrug** derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists/antagonists for reducing morbidity and risk of mortality from cardiovascular disease, breast cancer, and osteoporosis)

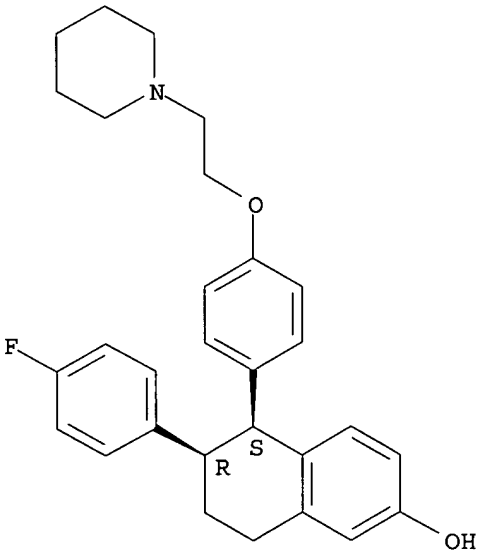
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



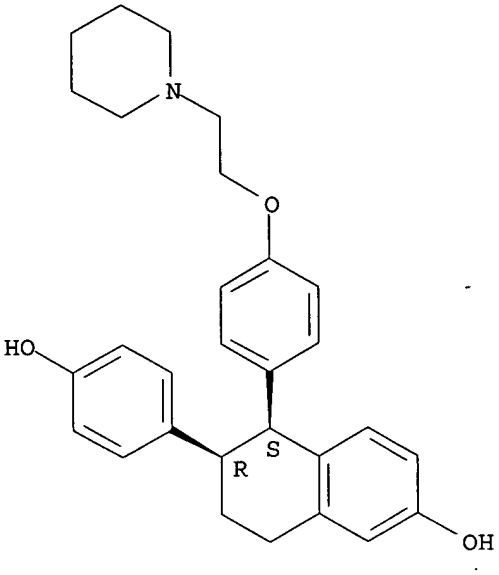
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

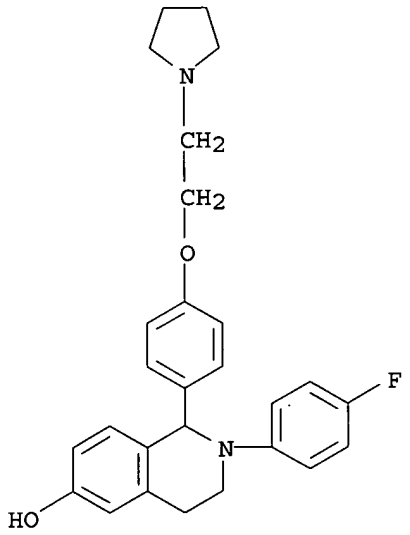


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

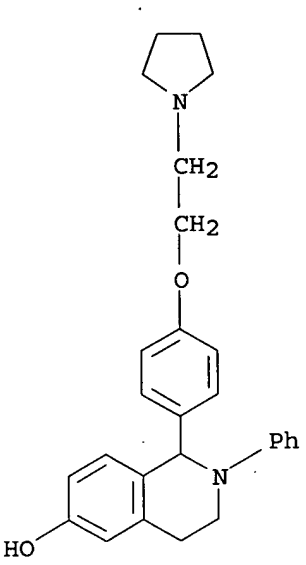
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

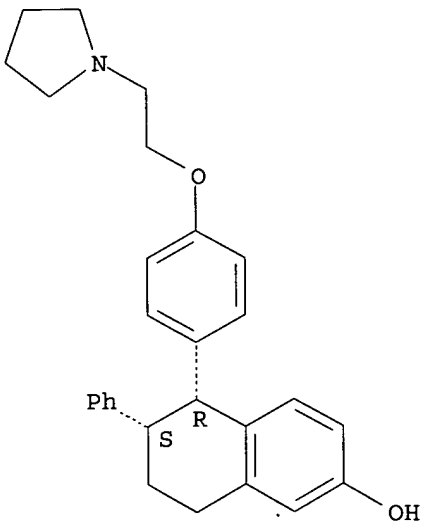


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



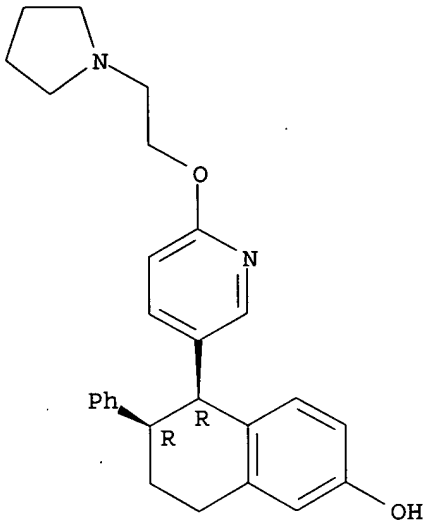
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L25 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:865154 HCAPLUS
DOCUMENT NUMBER: 134:21490
TITLE: Transdermal estrogen agonist-antagonist therapy
INVENTOR(S): Da Silva-Jardine, Paul Andrew
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1057480	A2	20001206	EP 2000-304611	20000530
EP 1057480	A3	20020109		
EP 1057480	B1	20040623		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001002588	A2	20010109	JP 2000-158026	20000529
CA 2310272	AA	20001201	CA 2000-2310272	20000530
ZA 2000002693	A	20011130	ZA 2000-2693	20000530
AT 269698	E	20040715	AT 2000-304611	20000530
ES 2220346	T3	20041216	ES 2000-304611	20000530
NZ 504868	A	20010928	NZ 2000-504868	20000531

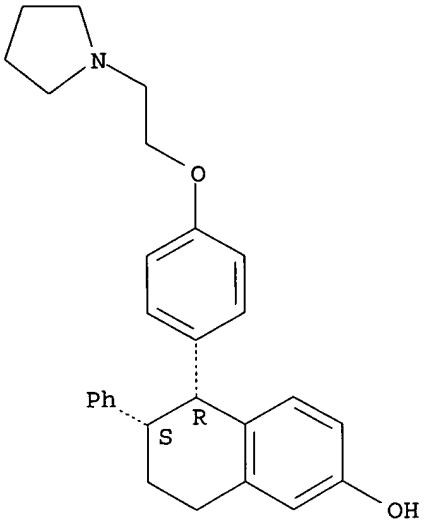
PRIORITY APPLN. INFO.: US 1999-137164P P 19990601
OTHER SOURCE(S): MARPAT 134:21490

AB Transdermal compns. for delivery of estrogen agonists-antagonists are effective in treating or preventing conditions related to estrogen imbalance. A transdermal patch was prepared containing (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol in a polymer matrix.

IT **180916-16-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal estrogen agonist-antagonist **therapy**)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:84288 HCAPLUS
DOCUMENT NUMBER: 132:132346
TITLE: A pharmaceutical composition for the prevention and treatment of diseases of cognitive dysfunction in a mammal
INVENTOR(S): Dasilva-Jardine, Paul A.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 976404	A2	20000202	EP 1999-305938		19990726
EP 976404	A3	20010627			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
MX 9907079	A	20000331	MX 1999-7079		19990729
BR 9903240	A	20000509	BR 1999-3240		19990729
JP 2000143541	A2	20000523	JP 1999-214965		19990729
PRIORITY APPLN. INFO.:			US 1998-94653P	P	19980730

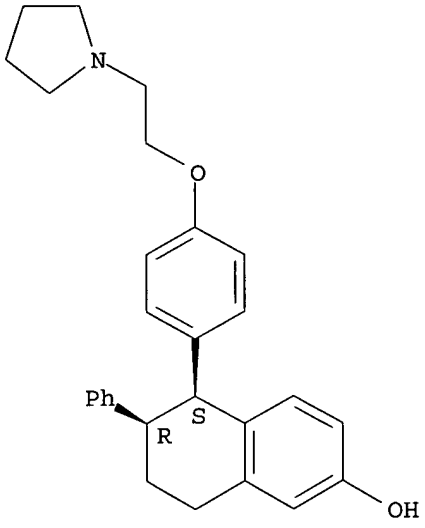
AB Pharmaceutical compns. for the treatment of diseases involving cognitive dysfunction in a mammal comprising an estrogen agonist or antagonist or a pharmaceutically acceptable salt thereof; an acetyl cholinesterase inhibitor or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier. The estrogen agonists or antagonists and acetylcholinesterase inhibitors are present in amts. that render the composition effective in the treatment of diseases of cognitive dysfunction

including Alzheimer's Disease and Dementia. The compns. may help memory enhancement. An example estrogen agonist or antagonist is droloxifene and an example acetylcholinesterase inhibitor is donepezil.

IT **180915-78-0 180915-84-8 180915-86-0**
180916-14-7 180916-15-8 193274-89-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** composition for the prevention and treatment of diseases of cognitive dysfunction in a mammal)

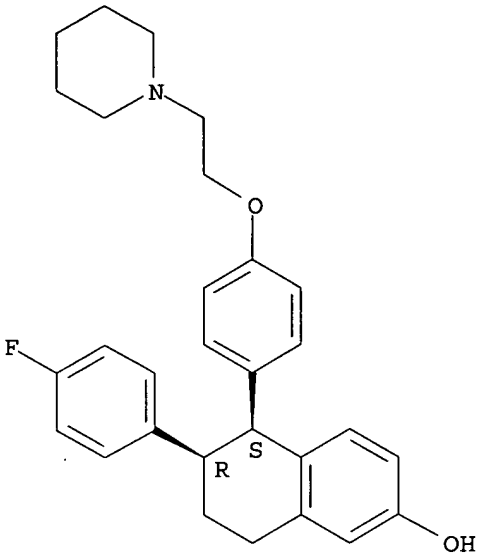
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



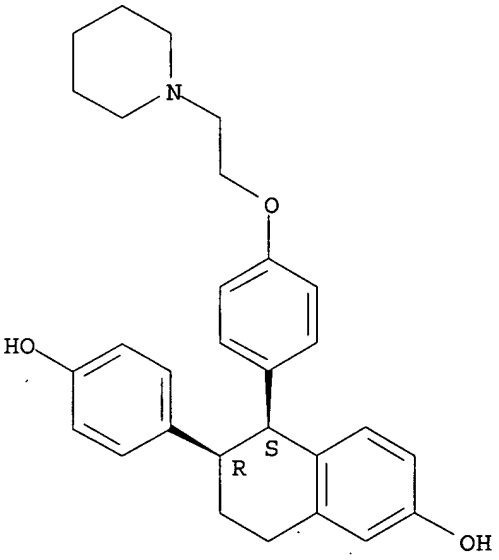
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

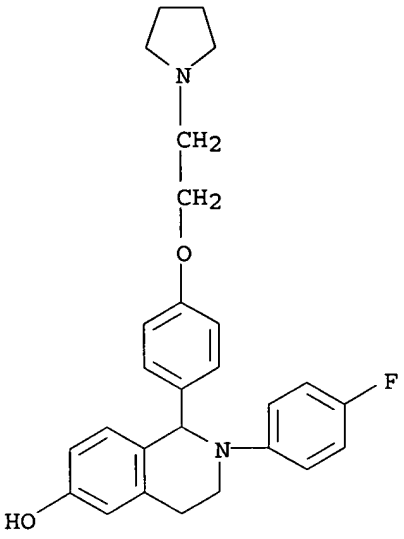


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

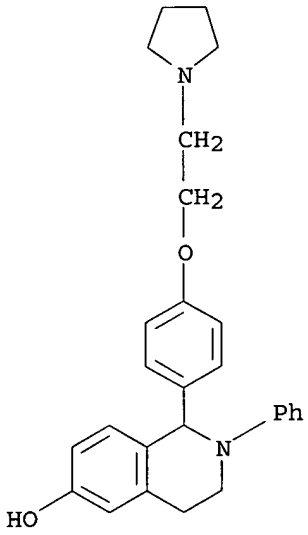
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

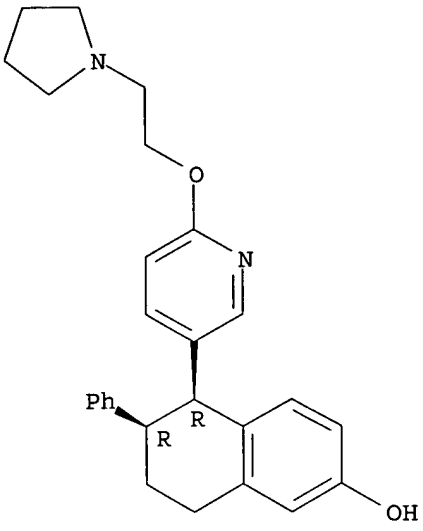


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L25 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:818996 HCAPLUS
DOCUMENT NUMBER: 132:44985
TITLE: Therapeutic combinations comprising a selective estrogen receptor modulator and prostaglandin E2
INVENTOR(S): Ke, Hua Zhu; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 966968	A1	19991229	EP 1999-304374	19990604
EP 966968	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 265853	E	20040515	AT 1999-304374	19990604
PT 966968	T	20040831	PT 1999-304374	19990604
ES 2220005	T3	20041201	ES 1999-304374	19990604
CA 2274381	AA	19991216	CA 1999-2274381	19990614
CA 2274381	C	20040210		
JP 2000026298	A2	20000125	JP 1999-167503	19990614
MX 9905564	A	20001130	MX 1999-5564	19990615
BR 9904146	A	20000509	BR 1999-4146	19990616
US 6284773	B1	20010904	US 1999-314371	19990714
PRIORITY APPLN. INFO.:			US 1998-89468P P	19980616

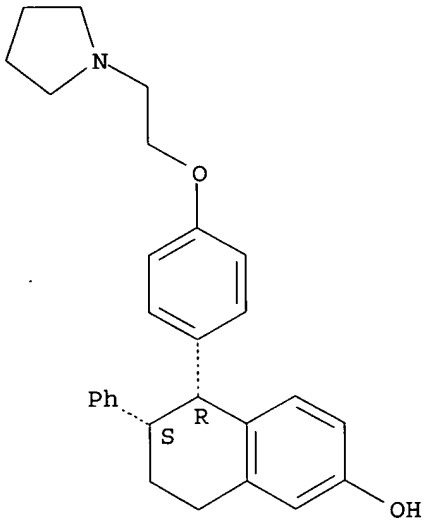
AB Combination compns. comprising (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol (I) or pharmaceutically acceptable salts and PGE2 or a pharmaceutically acceptable salt are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass and frailty. Expts. on rats show that I inhibits bone resorption and bone turnover, prevents further bone loss and preserves bone strength. Further I potentiates the

bone restoration effects of PGE2 in established osteopenic rats.

IT **180916-16-9 190791-29-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**therapeutic** combinations comprising a selective estrogen receptor modulator and prostaglandin E2)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

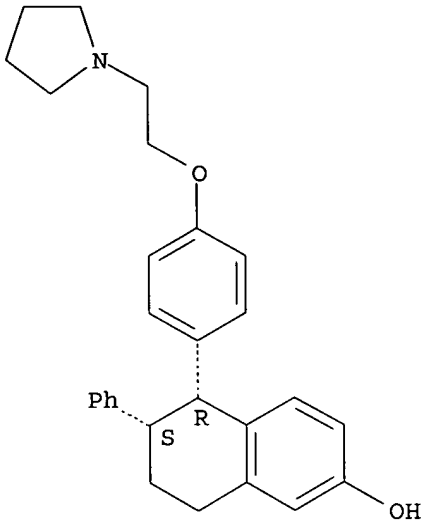


RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

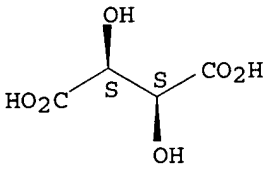
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:811078 HCAPLUS
DOCUMENT NUMBER: 132:45000
TITLE: Therapeutic combinations of (selective) estrogen receptor modulators (SERM) and growth hormone secretagogues (GHS) for treating musculoskeletal frailty
INVENTOR(S): Ke, Hua Zhu; Li, Mei; Pan, Lydia Codetta; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9965488 A1 19991223 WO 1999-IB796 19990503
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2335112 AA 19991223 CA 1999-2335112 19990503
AU 9933420 A1 20000105 AU 1999-33420 19990503
BR 9911357 A 20010313 BR 1999-11357 19990503
EP 1085867 A1 20010328 EP 1999-914723 19990503
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO
JP 2002518328 T2 20020625 JP 2000-554368 19990503
ZA 9903973 A 20001215 ZA 1999-3973 19990615
NO 2000006381 A 20001214 NO 2000-6381 20001214
HR 2000000857 A1 20011031 HR 2000-857 20001214
BG 105128 A 20011130 BG 2001-105128 20010108
PRIORITY APPLN. INFO.: US 1998-89424P P 19980616
WO 1999-IB796 W 19990503

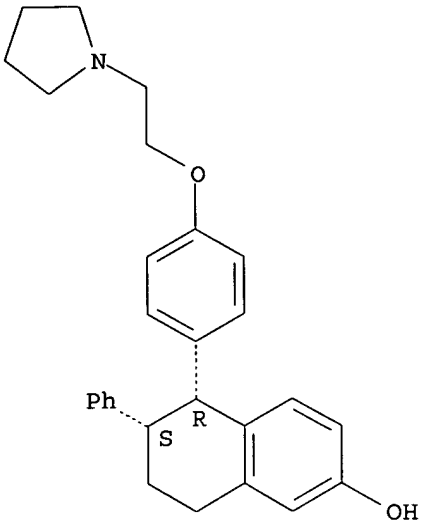
AB This invention is directed to pharmaceutical combination compns. and methods comprising (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)phenyl)-5,6,7,8-tetrahydronaphthalene-2-ol or a pharmaceutically acceptable salt thereof and 2-amino-N-(1(R)-(2,4-difluorobenzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydropyrazolo[4,3-c]pyridin-5-yl)ethyl-2-methylpropionamide or a pharmaceutically acceptable salt thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass, frailty and low muscle mass.

IT **180916-16-9 190791-29-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**therapeutic** combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

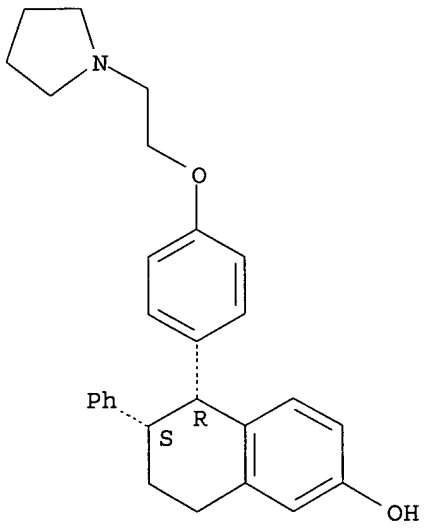


RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

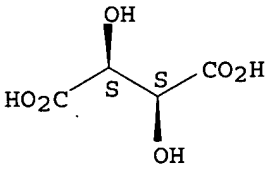
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:811077 HCAPLUS
DOCUMENT NUMBER: 132:44999
TITLE: Therapeutic combinations of (selective) estrogen receptor modulators (SERM) and growth hormone secretagogues (GHS) for treating musculoskeletal frailty
INVENTOR(S): Ke, Hua Zhu; Li, Mei; Pan, Lydia Codetta; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965486	A1	19991223	WO 1999-IB1117	19990616
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9903975	A	20001215	ZA 1999-3975	19990615
CA 2335134	AA	19991223	CA 1999-2335134	19990616
AU 9940547	A1	20000105	AU 1999-40547	19990616
BR 9911324	A	20010403	BR 1999-11324	19990616
EP 1087764	A1	20010404	EP 1999-923802	19990616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 200003544	T2	20010420	TR 2000-200003544	19990616
JP 2002518326	T2	20020625	JP 2000-554366	19990616
BG 105041	A	20010831	BG 2000-105041	20001211
NO 2000006312	A	20001212	NO 2000-6312	20001212
HR 2000000859	A1	20010430	HR 2000-859	20001214

PRIORITY APPLN. INFO.:		US 1998-89469P	P 19980616
		WO 1999-IB1117	W 19990616

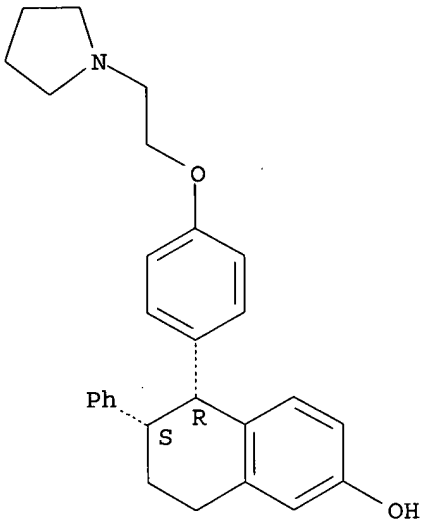
AB This invention is directed to pharmaceutical combination compns. and methods containing (-)-cis-6-phenyl-5-(4-(2-pyrrolidin-1-yl-ethoxy)phenyl)-5,6,7,8-tetrahydronaphtalene-2-ol or a pharmaceutically acceptable salt thereof and 2-amino-N-(2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-

hexahydropyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl)isobutyramide or a pharmaceutically acceptable salt thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass, frailty and low muscle mass.

IT **180916-16-9 252863-41-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**therapeutic** combinations of estrogen receptor modulators and growth hormone secretagogues for treating musculoskeletal frailty)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

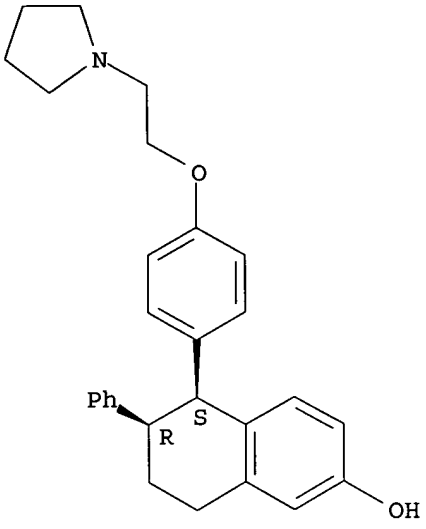


RN 252863-41-5 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180915-78-0
CMF C28 H31 N O2

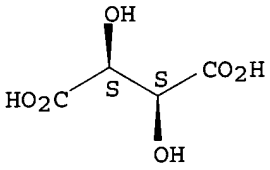
Relative stereochemistry.



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:811074 HCAPLUS
DOCUMENT NUMBER: 132:30842
TITLE: Therapeutic combinations comprising a selective estrogen receptor modulator and parathyroid hormone
INVENTOR(S): Ke, Hua Zhu; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965482	A1	19991223	WO 1999-IB949	19990526

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,

KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

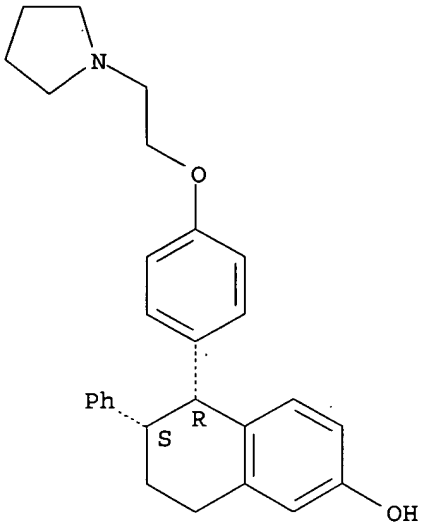
CA 2335078	AA	19991223	CA 1999-2335078	19990526
AU 9937259	A1	20000105	AU 1999-37259	19990526
BR 9911228	A	20010213	BR 1999-11228	19990526
EP 1094808	A1	20010502	EP 1999-919491	19990526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 200003567	T2	20010621	TR 2000-200003567	19990526
JP 2002518323	T2	20020625	JP 2000-554362	19990526
NZ 508039	A	20030328	NZ 1999-508039	19990526
ZA 9903972	A	20001215	ZA 1999-3972	19990615
US 6132774	A	20001017	US 1999-424010	19991115
NO 2000006313	A	20001212	NO 2000-6313	20001212
HR 2000000858	A1	20011031	HR 2000-858	20001214
BG 105125	A	20011130	BG 2001-105125	20010108
PRIORITY APPLN. INFO.:			US 1998-89479P P	19980616
			WO 1999-IB949 W	19990526

AB This invention is directed to pharmaceutical combination compns. and methods comprising (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol (I) or a pharmaceutically acceptable salt thereof and parathyroid hormone (PTH) or a biol. active fragment thereof, methods of using such compns. and kits containing such compns. The compns. are useful for treating musculoskeletal frailty, including osteoporosis, osteoporotic fracture, low bone mass and frailty. Data showed that combined treatment of PTH and I both restored bone mass and bone strength to established osteopenic, rats, and added extra cancellous bone to the proximal tibia and distal femur of the rats. I enhanced the bone restorative effects of PTH by a greated inhibition of bone resorption than bone formation.

IT **180916-16-9 190791-29-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**therapeutic** combinations comprising selective estrogen receptor modulator and parathyroid hormone)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

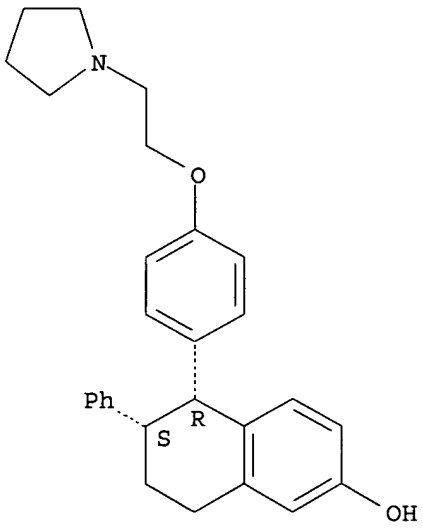


RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

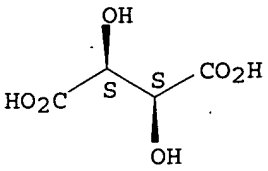
Absolute stereochemistry. Rotation (-).



CM 2

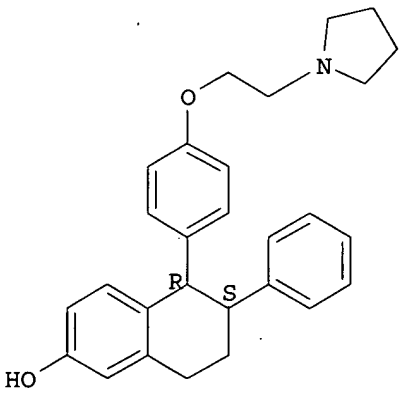
CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:450913 HCAPLUS
DOCUMENT NUMBER: 129:184100
TITLE: Discovery and Preclinical Pharmacology of a Novel, Potent, Nonsteroidal Estrogen Receptor Agonist/Antagonist, CP-336156, a Diaryltetrahydronaphthalene
AUTHOR(S): Rosati, Robert L.; Jardine, Paul Da Silva; Cameron, Kimberly O.; Thompson, David D.; Ke, Hua Zhu; Toler, Steven M.; Brown, Thomas A.; Pan, Lydia C.; Ebbinghaus, Charles F.; Reinhold, Anthony R.; Elliott, Nancy C.; Newhouse, Bradley N.; Tjoa, Christina M.; Sweetnam, Paul M.; Cole, Mark J.; Arriola, Mark W.; Gauthier, Jeffrey W.; Crawford, D. Todd; Nickerson, David F.; Pirie, Christine M.; Qi, Hong; Simmons, Hollis A.; Tkalcevic, George T.
CORPORATE SOURCE: Central Research Division, Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(16), 2928-2931
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

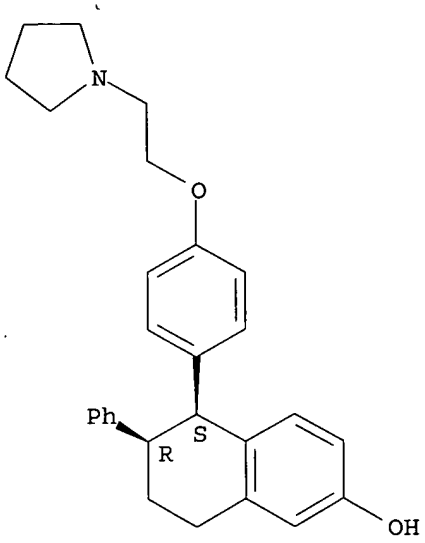
AB CP-336156 (I), a nonsteroidal estrogen agonist/antagonist with excellent oral bioavailability, was prepared and is as potent and efficacious as

estrogen at preventing bone loss and lowering total serum cholesterol in rats. In addition, estrogen-like proliferative effects on breast and uterine tissue were not observed The superior oral kinetics, achieved by minimizing intestinal glucuronidation through the application of a structural model, translated into a breakthrough for in vivo potency.

IT **180915-78-0P 180915-79-1P 180915-93-9P**
180916-16-9P, 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- **190791-29-8P**, CP-336156
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and preclin. **pharmacol.** of a potent, nonsteroidal estrogen agonist/antagonist, CP-336156)

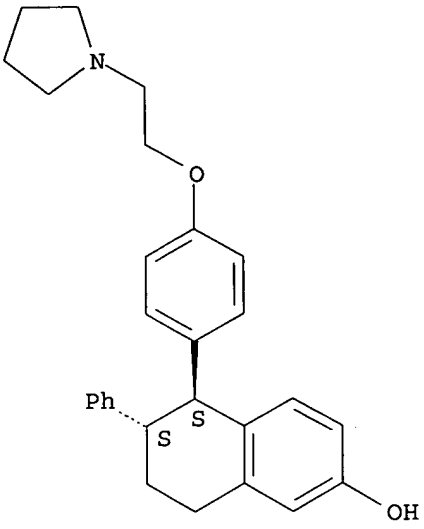
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



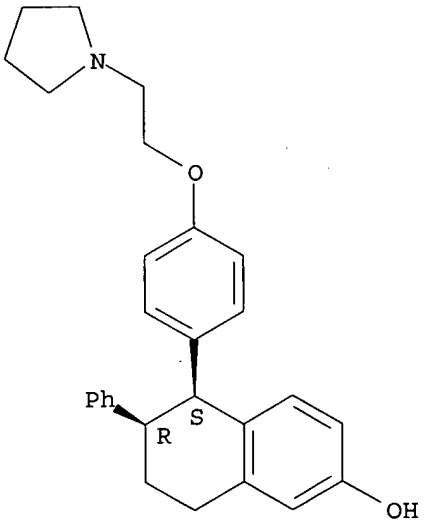
RN 180915-79-1 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



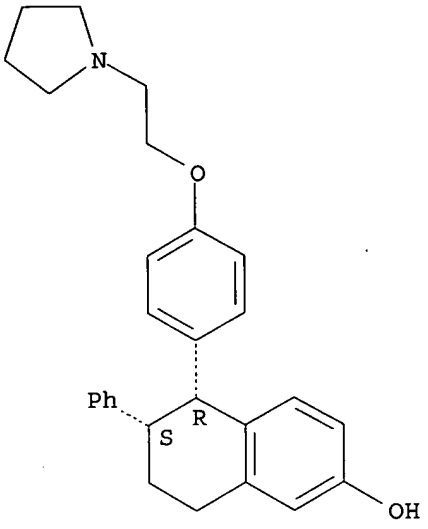
RN 180915-93-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

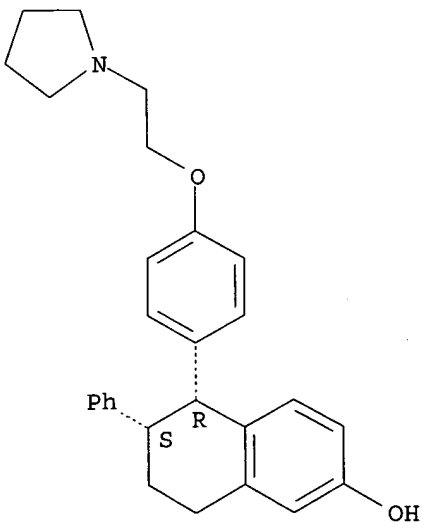


RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

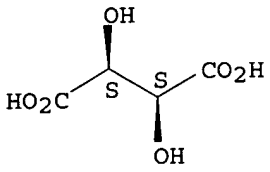
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:594636 HCAPLUS
DOCUMENT NUMBER: 127:257642
TITLE: Combination therapy for osteoporosis with estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists
INVENTOR(S): Ke, Hua Zhu; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731640	A1	19970904	WO 1996-IB1462	19961223
W: AU, BG, BR, BY, CA, CN, CZ, HU, IL, IS, JP, KR, KZ, LK, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 464496	B	20011121	TW 1996-85115770	19961220
CA 2247420	AA	19970904	CA 1996-2247420	19961223
AU 9710398	A1	19970916	AU 1997-10398	19961223
AU 703285	B2	19990325		
EP 883404	A1	19981216	EP 1996-941153	19961223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI, RO				
CN 1209064	A	19990224	CN 1996-180058	19961223
JP 11504352	T2	19990420	JP 1997-530738	19961223
BR 9612533	A	19990720	BR 1996-12533	19961223
NZ 323456	A	20010330	NZ 1996-323456	19961223
TR 9801679	T2	20010621	TR 1998-9801679	19961223
EP 1236475	A2	20020904	EP 2002-10920	19961223
EP 1236475	A3	20031105		
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RU 2190395	C2	20021010	RU 1998-117620	19961223
JP 2002308771	A2	20021023	JP 2002-54756	19961223
PL 187219	B1	20040630	PL 1996-328831	19961223
PL 187962	B1	20041130	PL 1996-359987	19961223
ZA 9701719	A	19980827	ZA 1997-1719	19970227
AP 975	A	20010612	AP 2000-200001962	19970227
W: BW, GM, KE, MW, UG, ZM, ZW				
AP 974	A	20010612	AP 1997-9700934	19970227

W: BW, GM, KE, MW, UG, ZM, ZW					
US 6323232	B1	20011127	US 1998-117972		19980811
NO 9803936	A	19980827	NO 1998-3936		19980827
US 2001009920	A1	20010726	US 2000-736051		20001213
AP 1179	A	20030630	AP 2002-2661		20021107
W: BW, KE, MW, UG, ZM, ZW					
PRIORITY APPLN. INFO.:			US 1996-12412P	P	19960228
			EP 1996-941153	A3	19961223
			JP 1997-530738	A3	19961223
			WO 1996-IB1462	W	19961223
			US 1998-117972	A3	19980811

OTHER SOURCE(S): MARPAT 127:257642

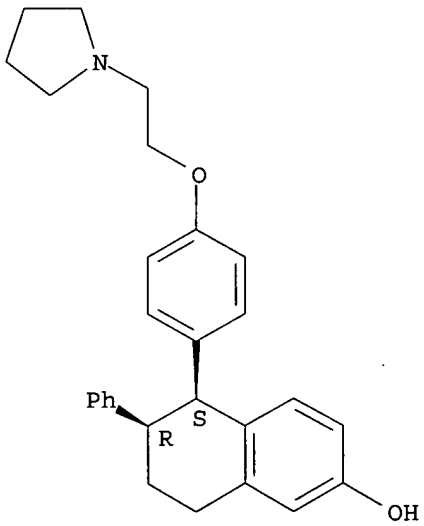
AB Pharmaceutical combination compns. are disclosed which include estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists. The compns. are useful for the treatment of bone disorders including osteoporosis. The effects of PGE2 and droloxifene on bone mineral content and bone mineral d. in ovariectomized rats were determined The data support the strategy of using an anabolic agent to restore bone mass, followed by an anti-resorptive agent to maintain the restored bone mass.

IT **180915-78-0 180915-84-8 180915-86-0**
180916-14-7 180916-15-8 180916-16-9
193274-89-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists/antagonists and prostaglandins or prostaglandin agonists/antagonists as combination **therapy** for bone disorders including osteoporosis)

RN 180915-78-0 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

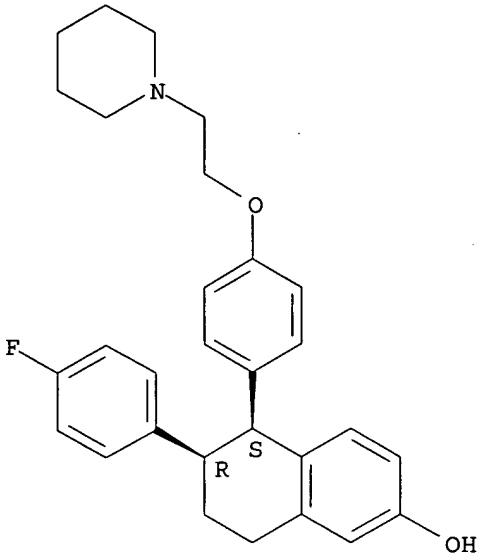
Relative stereochemistry.



RN 180915-84-8 HCAPLUS

CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 180915-86-0 HCAPLUS
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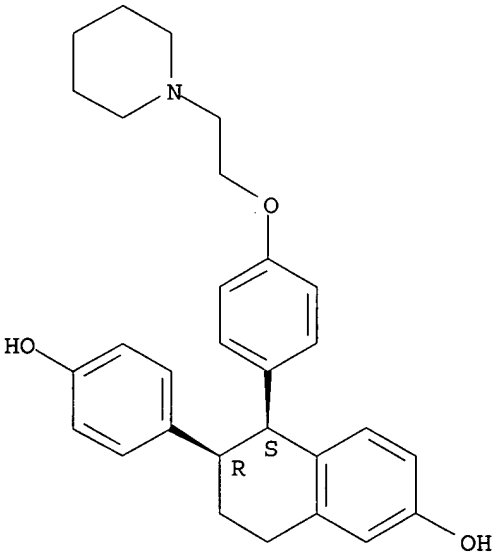
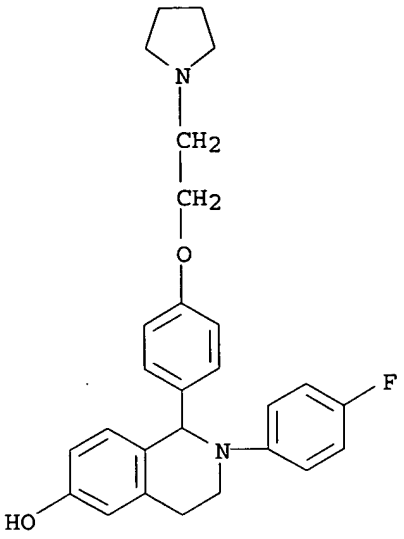
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



RN 180916-15-8 HCAPLUS
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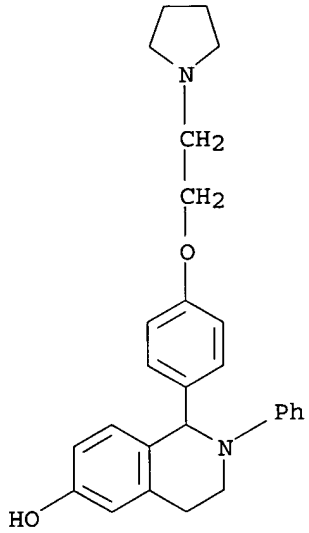
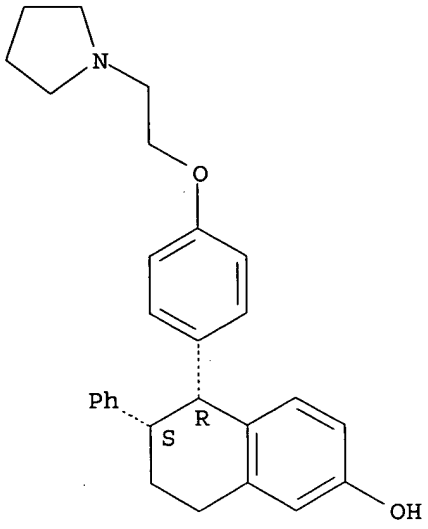


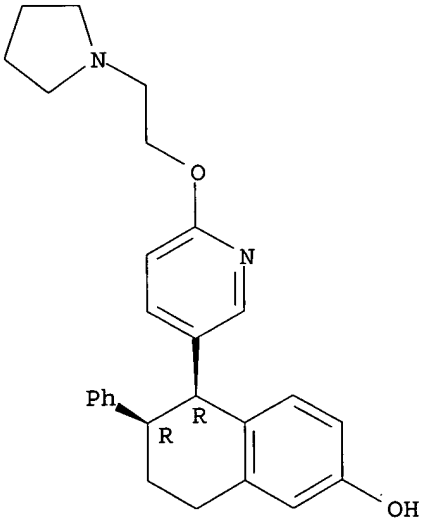
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



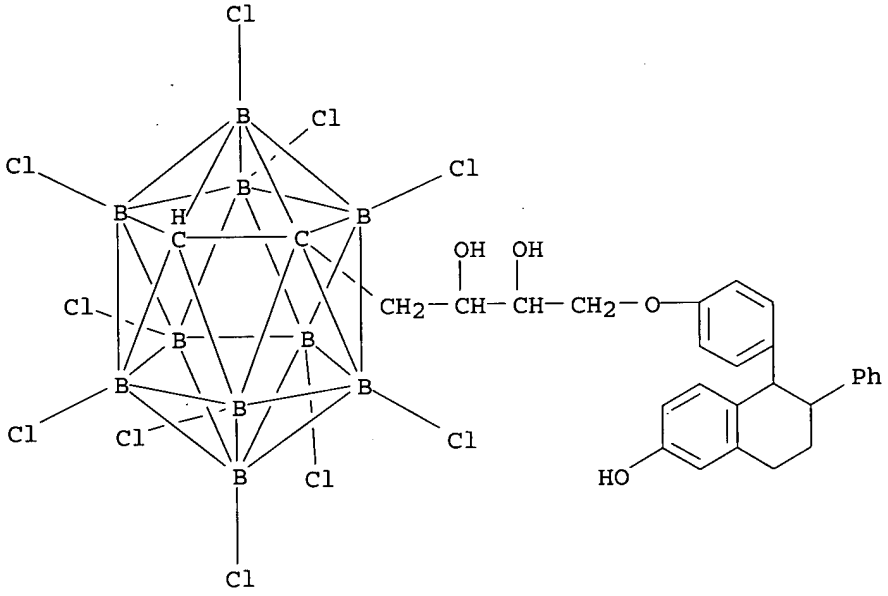
L25 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:537797 HCAPLUS
DOCUMENT NUMBER: 103:137797
TITLE: Boronated anti-estrogens for boron neutron capture therapy and boron neutron capture radiography
AUTHOR(S): Wellmann, Folkert; Gabel, Detlef
CORPORATE SOURCE: Dep. Chem., Univ. Bremen, Bremen, D-2800, Fed. Rep. Ger.
SOURCE: Brookhaven Natl. Lab., [Rep.] BNL (1983), BNL 51730, Proc. Int. Symp. Neutron Capture Ther., 1st, 276-80

CODEN: BNLRD9; ISSN: 0197-8659
DOCUMENT TYPE: Report
LANGUAGE: English

AB The synthesis of B-containing antiestrogens (U-23,469 and U-23,469-M) is described and an improved synthetic reaction scheme is presented. Uptake of U-23,469-M-Decloc by ZR75-1 cells, which contain estrogen receptors, was .apprx.105 mols./cell. Due to the low receptor concns. found in cells containing estrogen receptors, it is doubtful that steroids and their antagonists will be applicable in B-neutron capture therapy. They might be useful, however, in the in vivo measurement of receptor densities, or in neutron capture radiog.

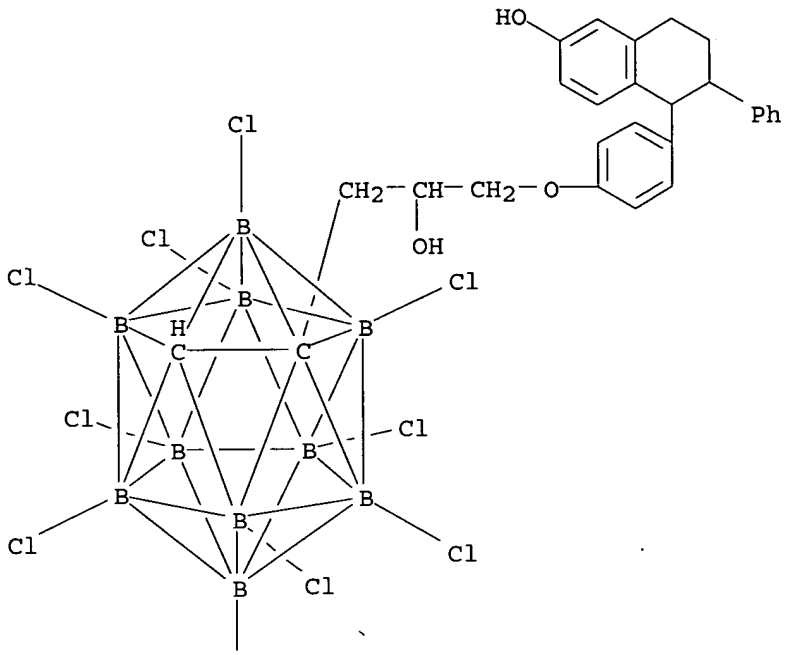
IT **98537-26-9P 98537-27-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as boronated antiestrogen for boron-neutron capture **radiotherapy** and radiog.)

RN 98537-26-9 HCAPLUS
CN 2,3-Butanediol, 1-(3,4,5,6,7,8,9,10,11,12-decachloro-1,2-dicarbadodecaboran(12)-1-yl)-4-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



RN 98537-27-0 HCAPLUS
CN 1,2-Dicarbadodecaborane(12)-1-ethanol, 3,4,5,6,7,8,9,10,11,12-decachloro-α-[[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

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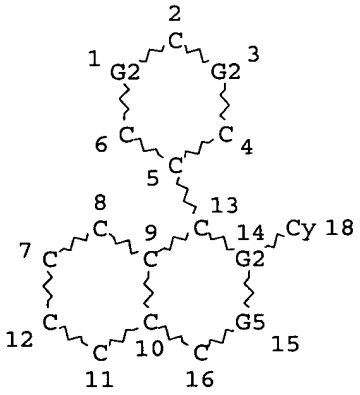
L7 SCR 1841
L14 STR



VAR G2=C/N
REP G5=(0-2) C
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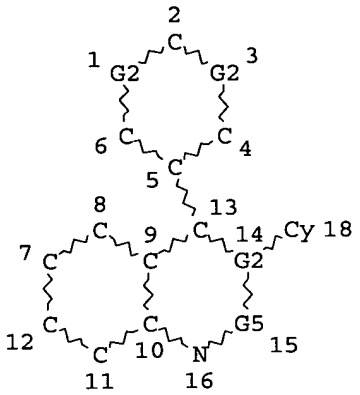
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L16 STR



VAR G2=C/N
REP G5=(0-2) C
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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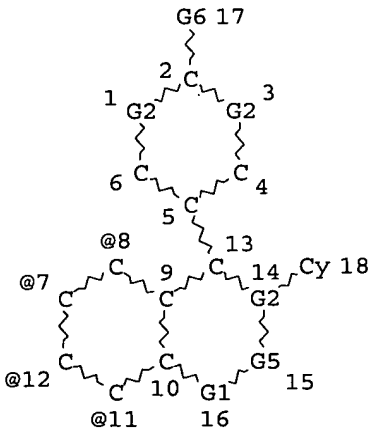
L22 STR



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@19 20 @21 22 23 @24 25 @26 27

OH @28

VAR G1=CH2/NH/19

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VAR G2=CH/N
VAR G3=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/21
REP G4=(3-4) C
REP G5=(0-2) C
VAR G6=CH2/24/26
VPA 28-7/8/11/12 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
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L24         130 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23
L25          33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24(L)(?MEDIC? OR ?THERAP? OR
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L26          58 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 AND (CARDIOVASCULAR
                DISEASE?/CV OR ATHEROSCLEROSIS?/CV OR HYPOGONADISM?/CV OR
                HYPERPLASIA?/CV OR OSTEOPOROSIS?/CV OR LIBIDO?/CV)
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                ?ATHEROSCL? OR ?HYPOGONAD? OR ?HYPERPLA? OR ?OSTEOPOR? OR
                ?LIBID?)
L28          37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L26 OR L27) NOT L25


=>
=>

=> d ibib abs hitstr l28 1-37

L28  ANSWER 1 OF 37  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:470251  HCAPLUS
DOCUMENT NUMBER:          143:19957
TITLE:                    Combination therapy comprising a cyclooxygenase 2
                          (COX-2) inhibitor and an antineoplastic agent for
                          treatment or prevention of neoplasia
INVENTOR(S):              Masferrer, Jaime L.
PATENT ASSIGNEE(S):       Pharmacia Corporation, USA
SOURCE:                   PCT Int. Appl., 317 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     --------------       ----   --------    --------------------    --------
     WO 2005048942         A2    20050602    WO 2004-US38019         20041115
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
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SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-519701P P 20031113

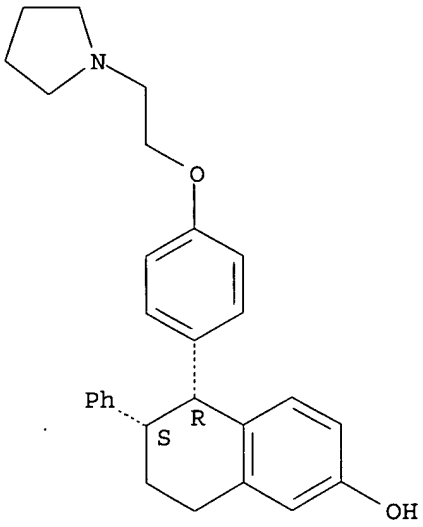
AB A method for treating or preventing neoplasia or a neoplasia-related disorder in a subject is provided, the method comprising administering to the subject an effective amount of a combination comprising a COX-2 inhibitor and an antineoplastic agent.

IT **180916-16-9**, Lasofoxifene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:198698 HCAPLUS

DOCUMENT NUMBER: 143:47

TITLE: Lasofoxifene: CP 336156, CP-336156

AUTHOR(S): Anon.

CORPORATE SOURCE: Adis International Ltd., Auckland, N. Z.

SOURCE: Drugs in R&D (2005), 6(1), 56-60
CODEN: DRDDFD; ISSN: 1174-5886

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Lasofoxifene [CP 336156] is a potent, nonsteroidal, tissue-selective estrogen receptor modulator (SERM). It has the bone-sparing and cardioprotective effects of estrogen, but lacks estrogen's uterine cancer risk. Lasofoxifene is under development with Ligand Pharmaceuticals and Pfizer (formerly Parke-Davis) for the prevention of postmenopausal osteoporosis and breast cancer. In June 2000, Parke-Davis' parent company, Warner-Lambert, merged with Pfizer. The resulting company retained the Pfizer name and Parke-Davis was integrated into Pfizer Global Research and Development. The discovery of lasofoxifene resulted from a research collaboration between Pfizer and

Ligand Pharmaceuticals. There was a contract dispute between the two companies relating to their research agreement. Under a settlement of litigation, Ligand is entitled to milestone and royalty payments. If Pfizer is successful in developing the drug through to regulatory approval in the US, Ligand could receive royalty revenues from lasofoxifene as early as 2003-2004. The royalties will be equal to 6% of net sales and will be in addition to milestone payments for continuing development of the drug. However, on 6 Mar. 2002, Ligand Pharmaceutical announced an agreement with Royalty Pharma in which the latter purchased the rights to a share of these future payments. Under the agreement, Ligand received $US6 million from Royalty Pharma in exchange for a 0.25% stake in net sales of three SERM products (lasofoxifene, bazedoxifene and bazedoxifene/Premarin) for a period of 10 years. Royalty Pharma retains the option to purchase, at escalating prices, addnl. rights (subject to timing restrictions) to extend this stake up to 1.0%, for a total of $US56 million. In Apr. 2002, Royalty Pharma exercised its first option to purchase an addnl. 0.125% of potential future sales of the three SERMS in exchange for $US3 million. Subsequently, in Dec. 2002, Royalty Pharma exercised an expanded option and agreed to pay Ligand $US6.775 million for 0.1875% of potential future sales of SERM products. Royalty Pharma and Ligand Pharmaceutical amended their royalty agreement in Oct. 2003 for the three SERM products. Under the amended agreement, Royalty Pharma exercised an option to pay Ligand $US 12.5 million, plus cumulative milestones of up to $US2.5 million upon the launches of the three SERMs (provided they are approved by 30 Sept. 2005), in exchange for 0.7% of potential future sales of the products for 10 years. In Nov. 2004, Ligand Pharmaceuticals and Royalty Pharma further amended their existing royalty agreement for the three SERM products. Under the terms of the revised agreement, Royalty Pharma will purchase an addnl. 1.625% of the SERM products' net sales for $US32.5 million, which represents an acceleration of the previous option timetable and an increase in the royalty amount as well as aggregate purchase price. Consequently, Royalty Pharma increased its rights to a total of 3.0125% of net sales of each SERM product for 10 years following the first com. sale of each product and has no further options. Ligand retains an approx. equal portion of lasofoxifene and other SERM's net sales going forward and for periods that could exceed 10 years. The royalty rates owed to Royalty Pharma for the royalties just purchased could be reduced by one-third if product sales exceed certain thresholds. Payments from the royalty purchase are non-refundable, regardless of whether the products ever become successfully launched or not. Milestone payments owed by Ligand's partners as products achieve development and regulatory targets will be paid to Ligand as earned and are not included in this amended agreement. In Sept. 2004, Ligand Pharmaceuticals earned a milestone payment of approx. $US2 million from Pfizer, payable in 181 818 shares of Ligand stock held by Pfizer. The payment was triggered by Pfizer's NDA submission for lasofoxifene in August 2004. Under the terms of the agreement between Ligand and Pfizer, Ligand is entitled to receive an addnl. milestone upon successful approval of lasofoxifene. On 19 August 2004, Pfizer filed an NDA with the US FDA for lasofoxifene for the prevention of osteoporosis in postmenopausal women. Product launch is forecasted to occur in 2006-2007. Ligand reported in Jan. 2004 at the 22nd Annual JP Morgan Healthcare Conference that it anticipated the availability of phase III data and NDA filing sometime in 2004. Lasofoxifene has undergone two phase III studies with Pfizer in the US as an orally administered therapy for postmenopausal osteoporosis. In June 2003, Pfizer reported that enrolment was completed in a trial evaluating lasofoxifene in the prevention of bone loss. The trial also evaluated lasofoxifene's effect on lipid levels. The trial enrolled 2≈000 postmenopausal women. Another trial was conducted among 8500 patients to investigate lasofoxifene in the treatment of

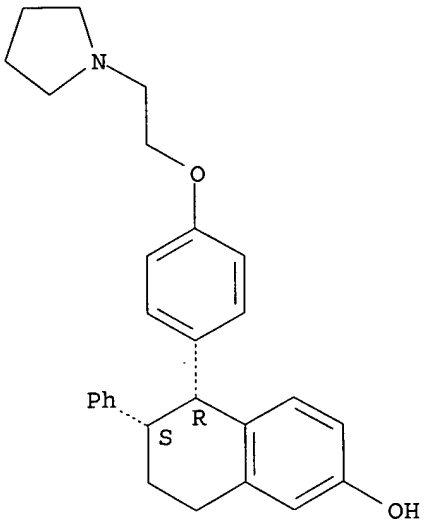
fractures. In addition, Pfizer began a third worldwide phase III trial to evaluate whether lasofoxifene reduced the risk of vertebral fractures, breast cancer and cardiovascular disease. At the 10th Annual Meeting of the Biotechnol. Industry Organization (BIO-2003), Ligand also confirmed that lasofoxifene was in phase III development for breast cancer. Lasofoxifene is under clin. evaluation as a treatment for vaginal atrophy. According to Pfizer's pipeline in Nov. 2004, the company anticipates regulatory submission for vaginal atrophy by the end of 2004. In June 2002, Ligand estimated that lasofoxifene has the potential to reach sales of $US1-2 billion, pending approval.

IT **180916-16-9**, Lasofoxifene
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CP-336156, CP-336156; lasofoxifene)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:55024 HCAPLUS
DOCUMENT NUMBER: 142:134783
TITLE: 17-Acetamido-4-azasteroid derivatives as androgen receptor modulators for the treatment of related diseases
INVENTOR(S): Dankulich, William P.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005004807	A2	20050120	WO 2004-US20753	20040625
WO 2005004807	A3	20050407		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483664P P 20030630
OTHER SOURCE(S): MARPAT 142:134783
GI

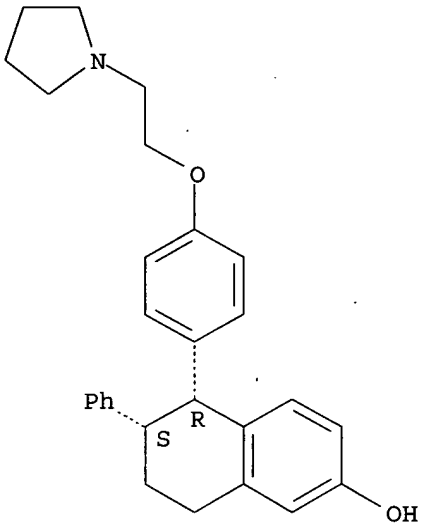
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Acetamido-4-azasteroid derivs., I (X = H or halogen; R1 = H, CF3, CO, C1-3 alkyl, C1-4 alkoxy, halogen , hydroxymethyl, wherein said alkyl, and alkoxy are optionally substituted with 1-7 F atoms; Y = a substituted or unsubstituted hetercycle containing at least one nitrogen; R2, R3 = H, halogen, C1-8 alkyl, aminoalkyl, hydroxycarbonyl, CN, OH, etc.) were prepared as androgen receptor modulators for the treatment of related diseases. Thus, II was treated with Et3N, and iso-Bu chloroformate, followed by LiBH4 to give the alchol. This alc. was converted to the tosylate, which was converted to the nitrile. Oxidation of the nitrile resulted in formation of the corresponding acid which was treated with 2-oxopiperizine, EDC, and HOAt to give III.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1050178 HCAPLUS
DOCUMENT NUMBER: 142:253438
TITLE: Lasofoxifene, a next generation estrogen receptor modulator: preclinical studies
AUTHOR(S): Maeda, Tomoko; Ke, Hua Zhu; Simmons, Hollis; Thompson, David
CORPORATE SOURCE: Tokyo Laboratories, Clinical Research, Pfizer Japan Inc. Pfizer Global Research and Development, Japan
SOURCE: Clinical Calcium (2004), 14(10), 1555-1563
CODEN: CLCCEJ; ISSN: 0917-5857
PUBLISHER: Iyaku Janarusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. Estrogen replacement therapy, in spite of efficacy in the prevention of osteoporotic fractures, has significant side effects and risks that limit its widespread usage in postmenopausal women. Thus significant medical need exists to find modalities that prevent osteoporosis, but without the side effects of estrogen. Selective estrogen receptor modulators (SERMs) have the potential to provide the skeletal benefits of estrogen without the increased risk of uterine and breast cancer. Tamoxifen, a first generation SERM is approved for the prevention and treatment of breast cancer, and raloxifene, a second generation SERM has been approved for the prevention and treatment of osteoporosis. Lasofoxifene, a new potent, nonsteroidal SERM, binds with high affinity to human estrogen receptors and acts as a tissue selective estrogen antagonist or agonist. In preclin. models of postmenopausal osteoporosis, lasofoxifene inhibited bone turnover and prevented bone loss throughout the skeleton. In studies designed to investigate the combination of lasofoxifene with estrogen, lasofoxifene blocked the hypertrophic effects of estrogen in the uterus, but did not block the bone protective effects. In immature and aged female rats, lasofoxifene did not affect the uterine weight and uterine histol. In preclin. studies designed to evaluate the effects of lasofoxifene on the uterus, a slight increase in wet uterine weight was observed in immature and aged female rats, but this difference was not observed in dry uterine weight suggesting that the increased uterine weight was due to increased water content in the tissue.

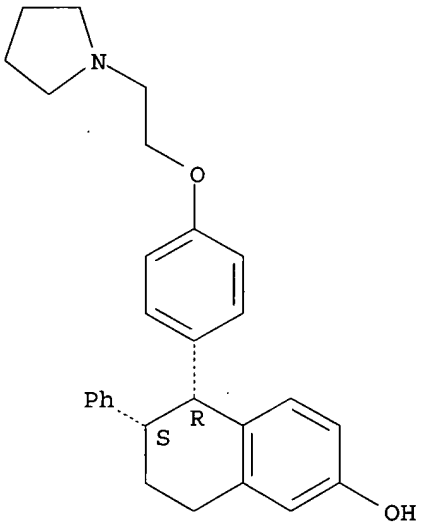
In preclin. studies designed to evaluate the effects of lasofoxifene in breast cancer, lasofoxifene inhibited breast tumor formation in mice injected with human MCF-7 breast cancer cells and in rats bearing mammary carcinomas. Thus, in preclin. models, lasofoxifene, a next generation SERM, prevents estrogen deficiency-induced bone loss, inhibits breast tumor formation, and reduces serum cholesterol, without causing uterine hypertrophy. These data suggest that lasofoxifene is a new potential therapy for the prevention of osteoporosis in postmenopausal women.

IT **180916-16-9**, Lasofoxifene
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene, a next generation estrogen receptor modulator for treatment of postmenopausal **osteoporosis**)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:995989 HCAPLUS
DOCUMENT NUMBER:	142:747
TITLE:	Combination treatment with strontium for the prophylaxis and/or treatment of cartilage and/or bone conditions
INVENTOR(S):	Hansen, Christian; Nilsson, Henrik
PATENT ASSIGNEE(S):	Nordic Bone A/S, Den.; Osteologix A/S; Christgau, Stephan
SOURCE:	PCT Int. Appl., 50 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098618	A2	20041118	WO 2004-DK327	20040506

WO 2004098618 A3 20050324
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

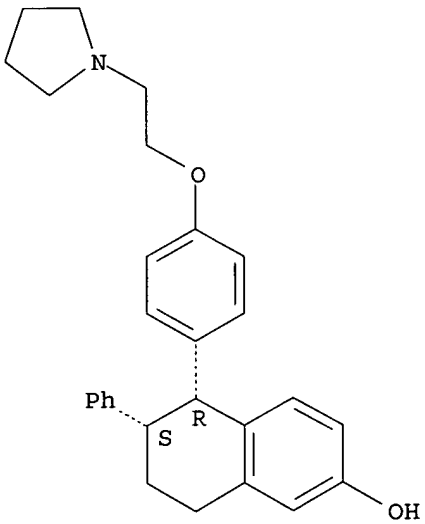
PRIORITY APPLN. INFO.:
DK 2003-691 A 20030507
DK 2003-931 A 20030620
DK 2003-1819 A 20031209
US 2003-528548P P 20031209

AB A combination treatment, wherein a strontium-containing compound together with one or more active substances capable of reducing the incidence of bone fracture and/or increasing bone d. and/or improving healing of fractured bone and/or improving bone quality are administered for use in the treatment and/or prophylaxis of cartilage and/or bone conditions.

IT **180916-16-9**, Lasofoxifene **190791-29-8**, CP-336156
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

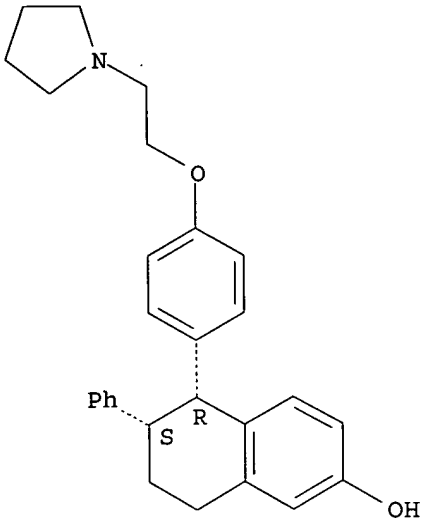


RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

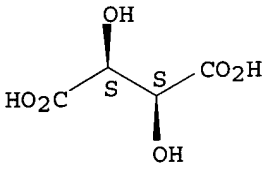
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



L28 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:683678 HCAPLUS
DOCUMENT NUMBER: 141:167568
TITLE: Pre- and postnatal development studies of lasofoxifene, a selective estrogen receptor modulator (SERM), in Sprague-Dawley rats
AUTHOR(S): Weisenburger, Walter P.; Hagler, Alan R.; Tassinari, Melissa S.
CORPORATE SOURCE: Pfizer Global Research and Development, Groton, CT, USA
SOURCE: Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2004), 71(3), 171-184
CODEN: BDRPCU; ISSN: 1542-9733
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lasofoxifene is a nonsteroidal selective estrogen receptor modulator

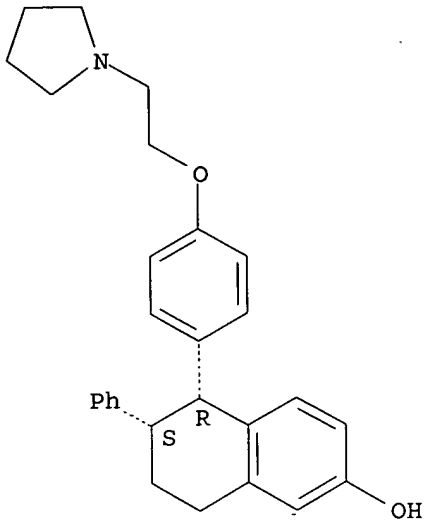
(SERM) developed for the treatment of postmenopausal osteoporosis. The purpose of these studies was to evaluate the effects of lasofoxifene on the postnatal development, behavior, and reproductive performance of offspring of female rats given lasofoxifene during organogenesis and lactation. Two range-finding studies were conducted to determine the effects of lasofoxifene at doses from 0.01-10 mg/kg on parturition and lactation in pregnant rats and on the early postnatal development of the offspring, and to optimize the dosing regimen. Maternal milk and blood plasma were sampled for concns. of lasofoxifene on Lactation Days 4, 7, and 14. In the pre- and postnatal development study, lasofoxifene was administered to pregnant and lactating rats by oral gavage at dose levels of 0.01, 0.03, and 0.1 mg/kg on Gestation Days 6-17 and Lactation Days 1-20. Maternal body weight and food consumption were measured throughout pregnancy, and body weight was measured throughout lactation. Parturition was monitored closely. The F1 offspring were measured for viability, body weight, anogenital distance, the appearance of postnatal developmental indexes and reflex behaviors, sensory function, in an age-appropriate functional observational battery, motor activity, auditory startle, passive avoidance, and the Cincinnati Water Maze. The F1 generation was assessed for reproductive function, and the F2 offspring were measured for body weight and viability throughout the lactation period. In the range-finding studies, indications of maternal toxicity included decreased body weight and food consumption, increased length of gestation, prolonged parturition, dystocia, and increased offspring mortality at birth. Concns. of lasofoxifene in maternal plasma were similar to those in milk, increased with increasing dose, and remained consistent over a 10-day period. In the pre- and postnatal development study, maternal body wts. and food consumption were decreased in all treated groups during gestation. Length of gestation was increased, parturition was prolonged, and dystocia was noted in the dams in the 0.1 mg/kg group. There was increased pup mortality in the F1 litters in the 0.1 mg/kg group and all treated groups had decreased offspring body wts. beginning at 1 wk of age, continuing into the postweaning period and, for the F1 males, into adulthood. Female F1 offspring in the 0.03 and 0.1 mg/kg groups had increased body wts. as adults. There were delays in the age of appearance of preputial separation in the males in the 0.1 mg/kg group and vaginal opening in the females in all treated groups. Body temperature was decreased by <0.5°C after weaning for male and female offspring in the 0.1 mg/kg group. The sensory, behavioral, and functional measures, including the tests of learning and memory, were unaffected by treatment. Mating success was lower for the F1 animals in the 0.1 mg/kg group, but there were no effects on the reproductive parameters. Mating, reproduction, and maternal behavior of the F1 animals in the 0.01 and 0.03 mg/kg groups and the survival and body wts. of the F2 offspring in all treated groups through Postnatal Day 21 were unaffected by treatment. The maternal findings in this study were related to the pharmacol. activity of lasofoxifene. Inhibition of growth of the F1 offspring after perinatal exposure to lasofoxifene was observed, but there were no significant effects on the sensory, behavioral, or functional measures, including learning and memory. There were no effects on the F2 generation. The findings are consistent with those reported for at least one other SERM. The findings of this study do not suggest increased risk for the primary indication of use in postmenopausal women.

IT **180916-16-9**, Lasofoxifene
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pre- and postnatal development studies of lasofoxifene in Sprague-Dawley rats)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:683677 HCAPLUS
DOCUMENT NUMBER: 141:167567
TITLE: Embryo/fetal toxicity assessment of lasofoxifene, a selective estrogen receptor modulator (SERM), in rats and rabbits
AUTHOR(S): Ozolins, T. R. S.; Gupta, U.
CORPORATE SOURCE: Department of Reproductive and Developmental Toxicity, Pfizer Global Research and Development, Safety Sciences, Groton, CT, USA
SOURCE: Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2004), 71(3), 161-170
CODEN: BDRPCU; ISSN: 1542-9733
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to evaluate the effects of lasofoxifene, a selective estrogen receptor modulator (SERM), on rat and rabbit fetal development. Lasofoxifene was administered orally to rats (1, 10, 100 mg/kg) between gestation days (GD) 6-17, and in rabbits (0.1, 1, 3 mg/kg) between GD 6-18. Maternal body weight and food consumption were monitored throughout pregnancy. Fetuses were delivered by Cesarean section on GD 21 in rats, and GD 28 in rabbits, to evaluate fetal viability, weight, and morphol. Drug concns. in maternal blood plasma were measured in a sep. cohort of animals at several time points commencing on GD 17 (rats) and 18 (rabbits). On GD 18 (rat) and GD 19 (rabbit) drug concns. were measured in maternal plasma and in fetal tissue 2 h post dosing to determine the fetal to maternal drug ratio. In rats, there were dose-related declines in maternal weight gain and food consumption. Post implantation loss was significantly increased at dosages of 10 and 100 mg/kg, and the number of viable fetuses was decreased at 100 mg/kg. The placental wts. increased, whereas fetal wts. decreased in a dose-dependent manner. Lasofoxifene-related teratol. findings were noted at 10 and 100 mg/kg and

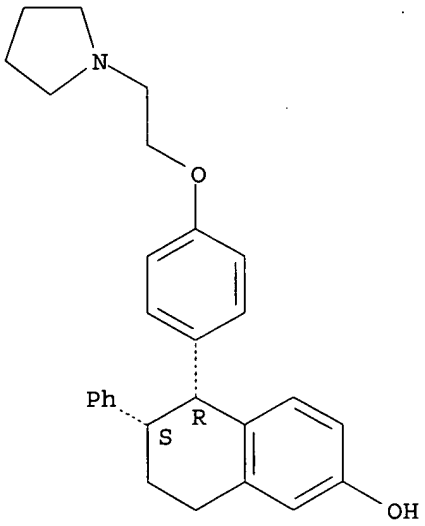
included imperforate anus with hypoplastic tails, dilatation of the ureters and renal pelvis, misaligned sternebrae, hypoflexion of hind-paw, wavy ribs, and absent ossification of sternebrae. In rabbits, neither maternal weight gain nor food consumption were affected during treatment. Between GD 26-28, there was a dose-dependent increased incidence of red discharge beneath the cages. At 1 and 3 mg/kg, resorptions and post-implantation loss increased. There were no significant external or visceral effects, but 3 mg/kg there was an increased incidence of supernumerary ribs. Although the maternal plasma Cmax and AUC(0-24) were dose-dependent, the exposures in the rat were many orders of magnitude greater than in the rabbit even for the same 1 mg/kg dose. The single time point fetal/maternal drug ratio was higher in the rat (1.3-0.78) than in the rabbit (0.21-0.16). In general, both maternal and fetal effects of lasofoxifene were similar to those reported with other SERMs. Although the incidence or severity of these effects was, in some instances, greater in the rat than in the rabbit, the doses and the resultant maternal and fetal exposures were many orders of magnitude higher in the rat, suggesting the rabbit to be more sensitive to the toxicol. effects of lasofoxifene.

IT **180916-16-9**, Lasofoxifene
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(embryo/fetal toxicity assessment of lasofoxifene in rats and rabbits)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:683676 HCAPLUS

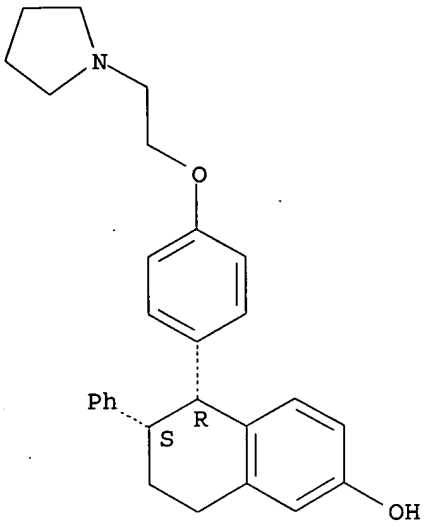
DOCUMENT NUMBER: 141:167566

TITLE: Reproductive toxicity assessment of lasofoxifene, a selective estrogen receptor modulator (SERM), in female rats

AUTHOR(S): Terry, K. K.; Cappon, G. D.; Hurtt, M. E.; Tassinari,

M. S.; Gupta, U.
CORPORATE SOURCE: Pfizer Global Research and Development, Groton, CT, USA
SOURCE: Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2004), 71(3), 150-160
CODEN: BDRPCU; ISSN: 1542-9733
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lasofoxifene is a nonsteroidal selective estrogen receptor modulator (SERM). With high affinity to the α and β human estrogen receptors and greater potency than other SERMs, lasofoxifene is potentially a superior treatment for postmenopausal osteoporosis. In light of the known effects of estrogen-modulating compds. on female reproductive indexes, 2 studies were conducted to evaluate the effects of lasofoxifene on female rat cyclicity, reproduction, and parturition. One study evaluated effects of lasofoxifene on estrous cyclicity, and the 2nd study assessed effects on implantation and parturition. In the cyclicity study, lasofoxifene was administered to female rats at doses of 0.1, 0.3, and 1.0 mg/kg/day for 14 consecutive days. After treatment, there was a 3-wk reversibility phase followed by a mating phase. In the implantation study, lasofoxifene was administered to pregnant female rats at doses of 0.01, 0.03, and 0.1 mg/kg/day for 7 consecutive days (gestation day [GD] 0-6). Some animals were euthanized on GD 21, and the remainder of the group was allowed to deliver the F1 generation. Several developmental indexes were evaluated in the F1 pups through post-natal day (PND) 21. In the cyclicity study, all lasofoxifene-treated females were anestrous by Study Day 7 (1.0 mg/kg) or 9 (0.3 and 0.1 mg/kg). The reversibility phase resulted in restoration of normal estrous cycles by the end of 1 (0.1 mg/kg) or 2 wk (0.3 and 1.0 mg/kg). During the mating phase, no adverse effects occurred in pregnancy success or reproductive parameters. In the implantation study, all doses of lasofoxifene increased pre- and post-implantation losses, increased gestation length, and reduced litter size. None of the developmental parameters measured on the F1 generation was adversely affected. Lasofoxifene reversibly altered the estrous cycle and inhibited implantation, consistent with what would be expected from a member of the SERM class.
IT **180916-16-9**, Lasofoxifene
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reproductive toxicity assessment of lasofoxifene in female rats)
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:683675 HCAPLUS
DOCUMENT NUMBER: 141:167565
TITLE: Reproductive toxicity assessment of lasofoxifene, a selective estrogen receptor modulator (SERM), in male rats
AUTHOR(S): Cappon, Gregg D.; Horimoto, Masao; Hurtt, Mark E.
CORPORATE SOURCE: Pfizer Global Research and Development, Groton, CT, USA
SOURCE: Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2004), 71(3), 142-149
CODEN: BDRPCU; ISSN: 1542-9733
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

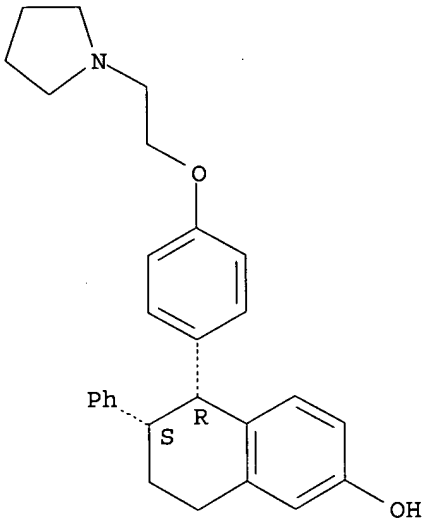
AB Lasofoxifene is a nonsteroidal selective estrogen receptor modulator (SERM) with greater than 100-fold selectivity against all other steroid receptors and is a potentially superior treatment for postmenopausal osteoporosis. The purpose of this study was to evaluate the effects of lasofoxifene on male reproduction in rats in light of the known effects of estrogen modulating compds. on male reproductive ability. Lasofoxifene was administered to adult male rats at doses of 0.1, 1, 10, and 100 mg/kg for 66-70 consecutive days. After 28 days of dosing, male rats were cohabited with untreated female rats. Female rats were euthanized on gestation day 14 and a uterine examination was carried out for evaluation of reproductive parameters and embryo viability. Male rats were euthanized after 66-70 days of dosing and epididymal sperm motility and concentration were assayed. The testes, epididymides, prostate, and seminal vesicles were weighed and microscopically examined The duration of cohabitation was increased for 100 mg/kg males by 0.7 days. The number of males copulating and the number of implantation sites produced per copulation were reduced in the 10 and 100 mg/kg groups. Wts. of the seminal vesicles and epididymides were reduced for all groups, although the testes weight and epididymal sperm motility and concentration were not affected by treatment. There were no microscopic findings in the male reproductive tissues. The

changes in male fertility and reproductive tissue wts. after exposure to lasofoxifene are consistent with those previously described for estrogen receptor-modulating compds.

IT **180916-16-9**, Lasofoxifene
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reproductive toxicity assessment of lasofoxifene in male rats)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:892539 HCAPLUS
DOCUMENT NUMBER: 139:375605
TITLE: Synthesis and uses of 4-azasteroid derivatives as selective androgen receptor modulators (SARMs)
INVENTOR(S): Wang, Jiabing; McVean, Carol A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092588	A2	20031113	WO 2003-US13120	20030425
WO 2003092588	A3	20040715		

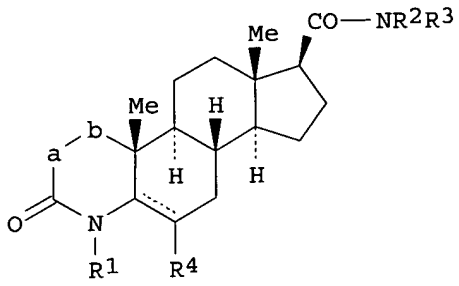
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2484173	AA	20031113	CA 2003-2484173		20030425
EP 1501512	A2	20050202	EP 2003-719957		20030425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005131005	A1	20050616	US 2003-512800		20030425
PRIORITY APPLN. INFO.:			US 2002-376779P	P	20020430
			WO 2003-US13120	W	20030425

OTHER SOURCE(S): MARPAT 139:375605

GI



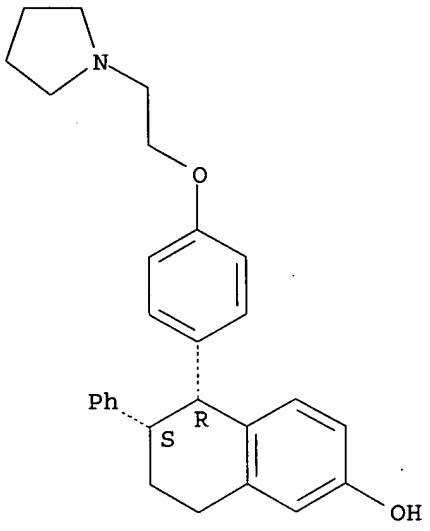
AB Compds. of structural formula (I) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in addition to SARMs treatment; synthesis and uses of 4-azasteroid derivs. as selective androgen receptor modulators (SARMs) in the treatment of androgen deficiency-related diseases)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:678670 HCAPLUS
DOCUMENT NUMBER: 139:192008
TITLE: Methods and composition for treating decreased libido in women with estrogenic components
INVENTOR(S): Coelingh Bennink, Herman Jian Tijmen
PATENT ASSIGNEE(S): Pantarhei Bioscience B.V., Neth.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070253	A1	20030828	WO 2003-NL125	20030219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

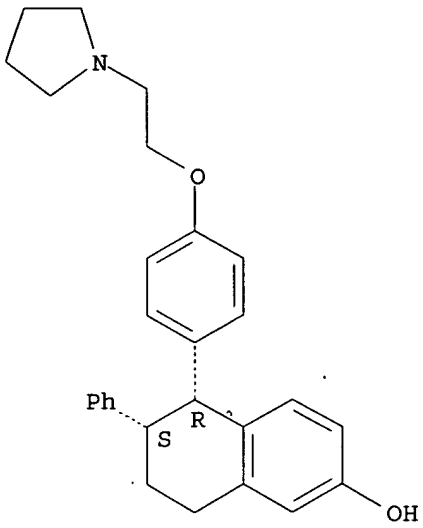
PRIORITY APPLN. INFO.: EP 2002-75696 A 20020221

AB The present invention is concerned with a method of treating decreased libido in pre-menopausal women, said decreased libido being the result of the repeated administration of a progestogenic component, wherein the method comprises the administration of the estrogenic component to a woman in an effective amount to improve the woman's libido. The present method is particularly suited for treating decreased libido in women using hormonal contraceptives that employ administration of a progestogenic component.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(methods and composition for treating decreased **libido** in women with estrogenic components)
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:610255 HCAPLUS
DOCUMENT NUMBER: 139:144410
TITLE: Treatment with selective estrogen receptor modulators (SERMs) in conjunction with progestins to suppress cartilage degeneration
INVENTOR(S): Christiansen, Claus; Christgau, Stephan
PATENT ASSIGNEE(S): Nordic Bioscience A/S, Den.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063859	A1	20030807	WO 2003-EP241	20030113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1465619 A1 20041013 EP 2003-702427 20030113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: GB 2002-743 A 20020114
US 2002-348730P P 20020114
GB 2002-9495 A 20020425
WO 2003-EP241 W 20030113

OTHER SOURCE(S): MARPAT 139:144410

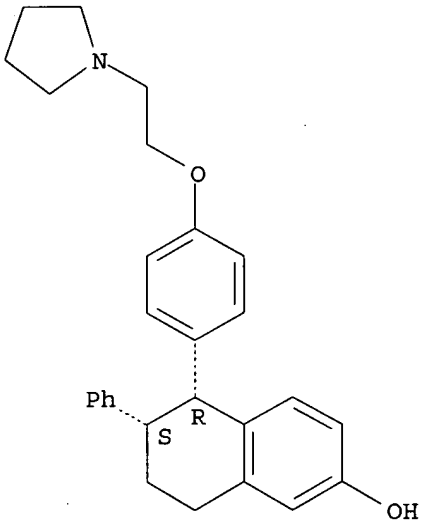
AB The present invention relates to the pharmaceutical use of selective estrogen receptor modulators (SERMs) alone or in combination with progestins for the treatment or prevention of diseases associated with elevated cartilage degradation In particular this invention relates to the pharmaceutical use of chroman derivs. in combination with moretindrone for the treatment or prevention of osteoarthritis or rheumatoid arthritis.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment with selective estrogen receptor modulators (SERMs) in conjunction with progestins to suppress cartilage degeneration)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:336422 HCAPLUS
DOCUMENT NUMBER: 139:316344
TITLE: Lasofoxifene (CP-336156), a novel selective estrogen receptor modulator, in preclinical studies
AUTHOR(S): Ke, H. Z.; Brown, T. A.; Thompson, D. D.
CORPORATE SOURCE: Osteoporosis Research, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, USA
SOURCE: Journal of the American Aging Association (2002), 25(2), 87-99

CODEN: JAAABY
PUBLISHER: Journal of the American Aging Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

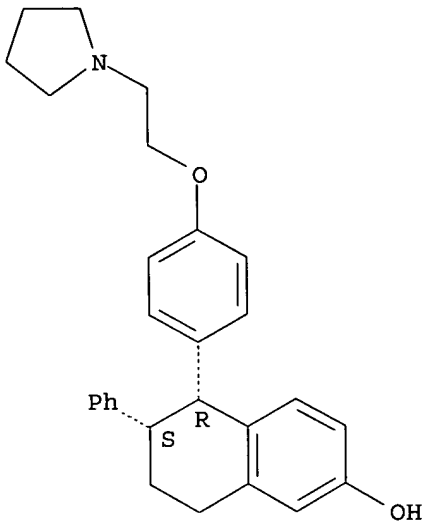
AB A review. Estrogen replacement therapy is reported to reduce the incidence of vertebral fractures in postmenopausal women, however, its compliance is limited because of side effects and safety concerns. Estrogen's side effects on breast and uterine tissues leading to the potential increased risk of uterine and breast cancer limit widespread estrogen usage. Thus, there is a significant medical need for a therapy that protects against postmenopausal bone loss but is free of estrogen's neg. effects on reproductive tissues. Selective estrogen receptor modulators (SERMs) have been investigated as an alternative to hormone replacement therapy. One such compound, raloxifene, has been approved for the prevention and treatment of osteoporosis. Lasofoxifene (LAS), a new, nonsteroidal, and potent SERM, is an estrogen antagonist or agonist depending on the target tissue. LAS selectively binds with high affinity to human estrogen receptors. In ovariectomized (OVX) rat studies, LAS prevented the decrease in femoral bone mineral d., tibial and lumbar vertebral trabecular bone mass at an ED100 of about 60 μg/kg/day. LAS inhibited the activation of trabecular and endocortical bone resorption and bone turnover in tibial metaphyses and diaphyses, and lumbar vertebral body in OVX rats. In addition, LAS decreased total serum cholesterol, inhibited body weight gain and increased soleus muscle weight in OVX rats. Similarly, LAS prevented bone loss induced by orchidectomy or aging in male rats by decreasing bone resorption and bone turnover while it had no effect in the prostate. Further, LAS decreased total serum cholesterol in intact aged male rats or in orchidectomized male rats. Synergestic skeletal effects were found with LAS in combination with bone anabolic agents such as prostaglandin E2 (PGE2), parathyroid hormone (PTH) or a growth hormone secretagogue (GHS) in OVX rats. In combination with estrogen, LAS inhibited the uterine stimulating effects of estrogen but did not block the bone protective effects of estrogen. In immature and aged female rats, LAS did not affect the uterine weight and uterine histol. In OVX adult female rats, LAS slightly but significantly increased uterine weight These results demonstrated that LAS produced effects on the skeleton indistinguishable from estrogen in female and male rats. However, unlike estrogen, LAS had little effect on uterine weight and cellular proliferation of uterus in female rats. In preclin. anti-tumor studies, LAS inhibited human breast cancer growth in mice bearing MCF7 tumors, prevented NMU-induced mammary carcinomas and possessed chemotherapeutic effects in NMU-induced carcinomas in rats. Therefore, we conclude that LAS possesses the antiestrogenic effects in breast tissue and estrogenic effects in bone and serum cholesterol, but lacks estrogen's side effects on uterine tissue. These data support the therapeutic potential of LAS for the prevention and treatment of postmenopausal bone loss and mammary carcinomas in humans.

IT **180916-16-9**, Lasofoxifene
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene (CP-336156), a novel selective estrogen receptor modulator, in preclin. studies)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

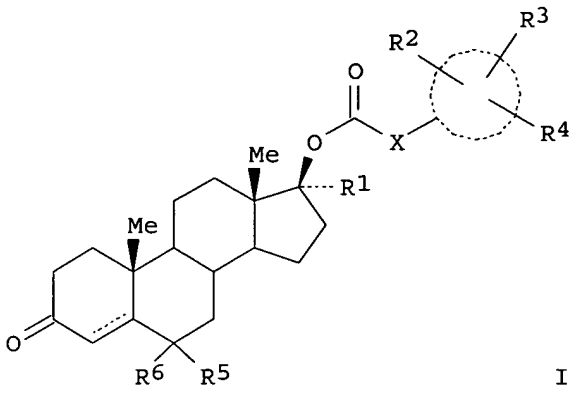
L28 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:261603 HCAPLUS
DOCUMENT NUMBER: 138:281598
TITLE: Androstane compounds as androgen receptor (AR) modulators for the treatment of AR-related diseases
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026568	A2	20030403	WO 2002-US29436	20020917
WO 2003026568	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459943	AA	20030403	CA 2002-2459943	20020917
EP 1429779	A2	20040623	EP 2002-766288	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005507886	T2	20050324	JP 2003-530207	20020917
US 2004235808	A1	20041125	US 2004-489072	20040308
PRIORITY APPLN. INFO.:			US 2001-324124P P	20010921

WO 2002-US29436 W 20020917

OTHER SOURCE(S): MARPAT 138:281598

GI



I

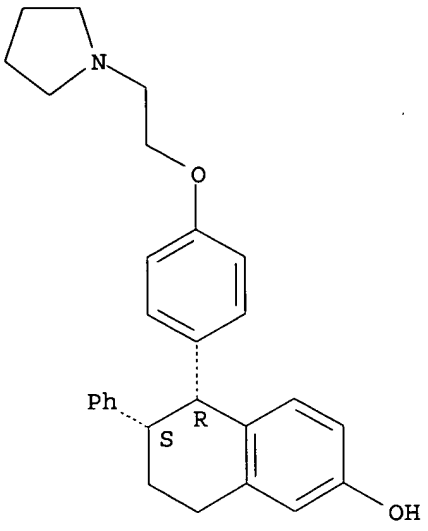
AB Compds. of structural formula (I) as herein defined are claimed as useful in a method for modulating a function of the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of activating the function of the androgen receptor in a patient, and in particular the method wherein the function of the androgen receptor is blocked in the prostate of a male patient or in the uterus of a female patient and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, female sexual dysfunction, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active agents. Methods for the co-administration of those compds. with bone-strengthening agents are also claimed.

IT **180916-16-9**, Lasofoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androstane compds. as androgen receptor (AR) modulators in conjunction with bone-strengthening agents for treatment of AR-related diseases)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:117617 HCAPLUS
DOCUMENT NUMBER: 138:147771
TITLE: Pharmaceutical compositions, kits and methods comprising combinations of estrogen agonists/antagonists, estrogens and progestins
INVENTOR(S): Ke, Hua Zhu; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011282	A1	20030213	WO 2002-IB2763	20020704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2448235	AA	20030213	CA 2002-2448235	20020704
NZ 529511	A	20031219	NZ 2002-529511	20020704
EP 1411922	A1	20040428	EP 2002-743537	20020704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504032	T2	20050210	JP 2003-516512	20020704
US 2003065017	A1	20030403	US 2002-206587	20020726
ZA 2003008809	A	20041123	ZA 2003-8809	20031112

PRIORITY APPLN. INFO.: US 2001-309065P P 20010731
WO 2002-IB2763 W 20020704

AB The present invention relates to pharmaceutical compns., kits and methods comprising combinations of lasofoxifene ((-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol) or nontoxic pharmacol. acceptable acid addition salts thereof and estrogens. The present invention also relates to pharmaceutical compns., kits and methods comprising combinations of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6, 7 ,8-tetrahydro-naphthalene-2-ol or nontoxic pharmacol. acceptable acid addition salts thereof, estrogens and progestins. In the examples provided, lasofoxifene tartrate alone or in combination with 17β-ethynylestradiol completely reversed ovariectomy-induced bone loss in rats and antagonized the uterine hypertrophy effects induced by the estrogen.

IT **190791-29-8**, Lasofoxifene tartrate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene, estrogen and progestin for treatment of **osteoporosis** and sexual dysfunctions)

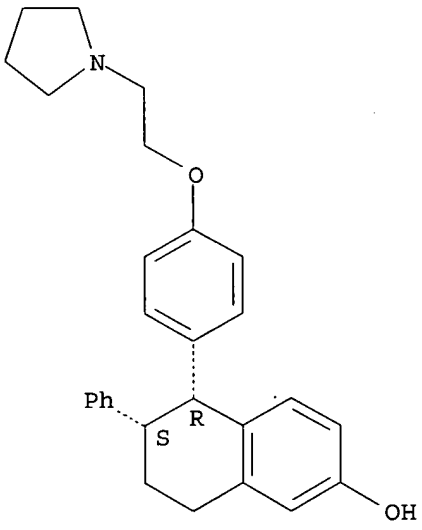
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

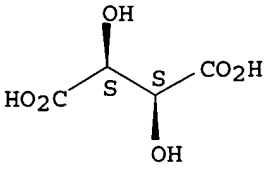
Absolute stereochemistry. Rotation (-).



CM 2

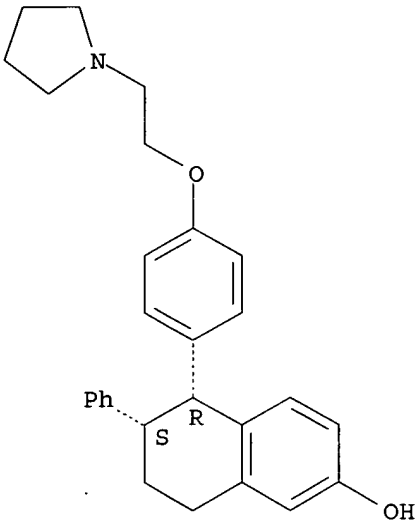
CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



IT **180916-16-9**, Lasofoxifene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene, estrogen and progestin for treatment of **osteoporosis** and sexual dysfunctions)
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:449656 HCAPLUS
DOCUMENT NUMBER: 137:47127
TITLE: Preparation of isoquinolines and isoindolines as selective estrogen receptor-β ligand
INVENTOR(S): Barlaam, Bernard; Dantzman, Cathy
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046164	A1	20020613	WO 2001-SE2724	20011207

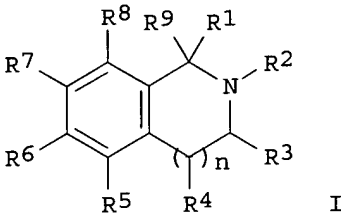
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

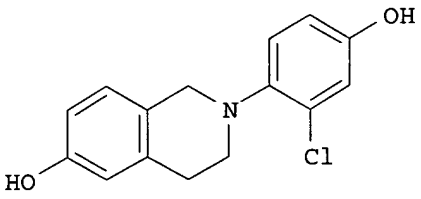
AU 2002022853	A5	20020618	AU 2002-22853	20011207
EP 1341765	A1	20030910	EP 2001-999560	20011207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004515494	T2	20040527	JP 2002-547903	20011207
US 2005101584	A1	20050512	US 2003-450023	20011207
PRIORITY APPLN. INFO.:			US 2000-251775P	P 20001207
			US 2000-251779P	P 20001207
			SE 2001-6	A 20010102
			SE 2001-7	A 20010102
			WO 2001-SE2724	W 20011207

OTHER SOURCE(S): MARPAT 137:47127

GI



I



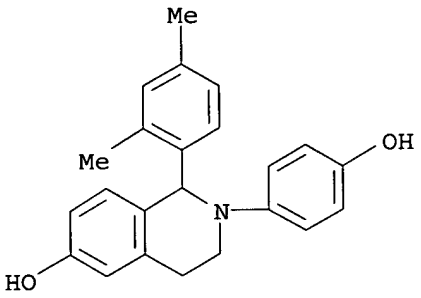
II

AB Title compds. I [R1 = H, (un)substituted-alkyl, -Ph, or -R10; R2 = (un)substituted-alkyl, -Ph, -PhCO, -benzyl or -R10; R3 = H, alkyl, Ph(CH2)m or R10(CH2)m; R4 = R3, halo; R5 and R8 independently = halo, CN, nitro, haloalkyl, R11, R11O, R11S, R112N, R11O2C, R11C(=O)O, R112NCO, R11COR11N, unsubstituted alkyl, etc.; R6 and R7 independently = halo, CN, nitro, haloalkyl, R11, R11O, R11S, R112N, R11O2C, R11C(=O)O, R112NCO, R11COR11N, etc. ; R10 = (un)substituted 5 or 6-membered heterocycle possessing 0-1 oxo groups and/or 0-1 fused benzo rings; R11 = H, alkyl, haloalkyl, Ph or benzyl; m = 0-3; n = 0-1] are prepared and claimed, with their pharmaceutically acceptable salts, as selective estrogen receptor-β ligands. Thus, II was prepared by N-arylation of 6-methoxy-1,2,3,4-tetrahydroisoquinoline with 4-bromo-3-chloroanisole with subsequent boron tribromide deetherification. In estrogen receptor binding assays, I demonstrated Ki values for β-ER in the range of 1.2-459 (nM). As selective ER-β ligands, I are useful in the treatment or prophylaxis of Alzheimer's disease, anxiety disorders, depressive disorders, osteoporosis, cardiovascular disease, rheumatoid

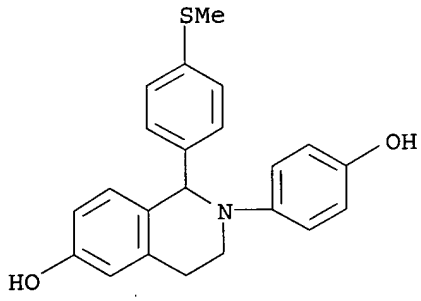
arthritis or prostate cancer.

IT **436856-45-0P 436856-47-2P 436856-53-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of isoquinolines and isoindolines as selective estrogen receptor-β ligands)

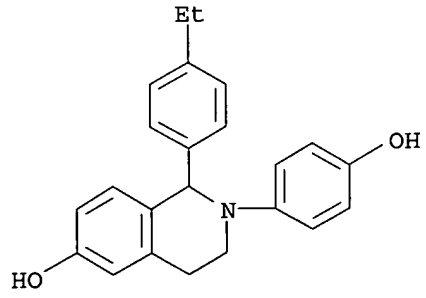
RN 436856-45-0 HCAPLUS
CN 6-Isoquinolinol, 1-(2,4-dimethylphenyl)-1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 436856-47-2 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)-1-[4-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



RN 436856-53-0 HCAPLUS
CN 6-Isoquinolinol, 1-(4-ethylphenyl)-1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:274749 HCAPLUS
DOCUMENT NUMBER: 135:205314
TITLE: Lasofoxifene (CP-336,156) protects against the age-related changes in bone mass, bone strength, and total serum cholesterol in intact aged male rats
AUTHOR(S): Ke, Hua Zhu; Qi, Hong; Chidsey-Frink, Kristin L.; Crawford, D. Todd; Thompson, David D.
CORPORATE SOURCE: Osteoporosis Research, Department of Cardiovascular and Metabolic Diseases, Global Research and Development, Pfizer, Incorporated, Groton, CT, USA
SOURCE: Journal of Bone and Mineral Research (2001), 16(4), 765-773
CODEN: JBMREJ; ISSN: 0884-0431
PUBLISHER: American Society for Bone and Mineral Research
DOCUMENT TYPE: Journal
LANGUAGE: English

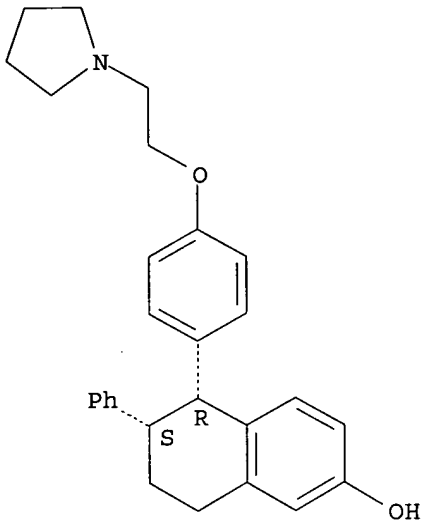
AB The purpose of this study was to evaluate if long-term (6 mo) treatment with lasofoxifene (LAS), a new selective estrogen receptor modulator (SERM), can protect against age-related changes in bone mass and bone strength in intact aged male rats. Sprague-Dawley male rats at 15 mo of age were treated (daily oral gavage) with either vehicle (n = 12) or LAS at 0.01 mg/kg per day (n = 12) or 0.1 mg/kg per day (n = 11) for 6 mo. A group of 15 rats was necropsied at 15 mo of age and served as basal controls. No significant change was found in body weight between basal and vehicle controls. However, an age-related increase in fat body mass (+42%) and decrease in lean body mass (-8.5%) was observed in controls. Compared with vehicle controls, LAS at both doses significantly decreased body weight and fat body mass but did not affect lean body mass. No significant difference was found in prostate wet weight among all groups. Total serum cholesterol was significantly decreased in all LAS-treated rats compared with both the basal and the vehicle controls. Both doses of LAS treatment completely prevented the age-related increase in serum osteocalcin. Peripheral quant. computerized tomog. (pQCT) anal. at the distal femoral metaphysis indicated that the age-related decrease in total d., trabecular d., and cortical thickness was completely prevented by treatment with LAS at 0.01 mg/kg per day or 0.1 mg/kg per day. Histomorphometric anal. of proximal tibial cancellous bone showed an age-related decrease in trabecular bone volume (TBV; -46%), trabecular number (Tb.N), wall thickness (W.Th), mineral apposition rate, and bone formation rate-tissue area referent. Moreover, an age-related increase in trabecular separation (Tb.Sp) and eroded surface was observed LAS at 0.01 mg/kg per day or 0.1 mg/kg per day completely prevented these age-related changes in bone mass, bone structure, and bone turnover. Similarly, the age-related decrease in TBV and trabecular thickness (Tb.Th) and the age-related increase in osteoclast number (Oc.N) and osteoclast surface (Oc.S) in the third lumbar vertebral cancellous bone were completely prevented by treatment with LAS at both doses. Further, LAS at both doses completely prevented the age-related decrease in ultimate strength (-47%) and stiffness (-37%) of the fifth lumbar vertebral body. These results show that treatment with LAS for 6 mo in male rats completely prevents the age-related decreases in bone mass and bone strength by inhibiting the increased bone resorption and bone turnover associated with aging. Further, LAS reduced total serum cholesterol and did not affect the prostate weight in these rats. Our data support the potential use of a SERM for protecting against the age-related changes in bone and serum cholesterol in elderly men.

IT **180916-16-9**, Lasofoxifene

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lasofoxifene (CP-336,156) protects against age-related changes in bone mass, bone strength, and total serum cholesterol in intact aged male rats)

RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:123186 HCAPLUS
DOCUMENT NUMBER: 134:173020
TITLE: Drugs containing estrogen agonists for treatment of osteoporosis, cardiovascular diseases, and breast cancer
INVENTOR(S): Yu, Julia Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001048805	A2	20010220	JP 2000-222159	20000724
EP 1086692	A2	20010328	EP 2000-305611	20000703
EP 1086692	A3	20030709		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 2000048827	A5	20010201	AU 2000-48827	20000725
CA 2314572	AA	20010128	CA 2000-2314572	20000726

NZ 506014	A	20011130	NZ 2000-506014	20000727
PRIORITY APPLN. INFO.:			US 1999-146072P P	19990728
			US 1999-146075P P	19990728

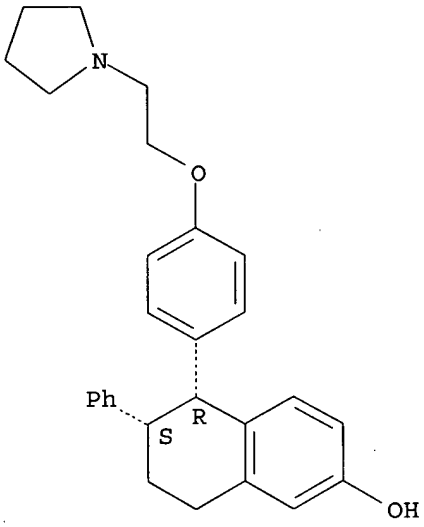
AB Prophylactic and/or therapeutic agents, which can treat the title diseases in patients undergoing therapy with warfarin (I) or propranolol (II) without affecting actions of I or II, contain estrogen agonists such as lasofoxifene (III) and droloxifene (IV). Bindings of I and II by human plasma proteins were not affected by III or IV. Administration of III to 12,000 ≥60-yr-old women with high risk of breast cancer significantly prevented breast cancer.

IT **180916-16-9**, Lasofoxifene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of **osteoporosis**, cardiovascular diseases, and breast cancer with estrogen agonists which do not interact with warfarin or propranolol)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2000:833287 HCAPLUS
DOCUMENT NUMBER:	134:4858
TITLE:	Preparation of cis-1-[2-[4-(6-methoxy-2-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine as intermediate for antiosteoporotic agent
INVENTOR(S):	Chu, Charles Kuok Fang
PATENT ASSIGNEE(S):	Pfizer Products Inc., USA
SOURCE:	Jpn. Kokai Tokkyo Koho, 7 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000327670	A2	20001128	JP 2000-152901	20000524
JP 3296809	B2	20020702		
CN 1280128	A	20010117	CN 2000-108576	20000518
CN 1502597	A	20040609	CN 2003-10119667	20000518
CN 1502598	A	20040609	CN 2003-10119668	20000518
CA 2308922	AA	20001124	CA 2000-2308922	20000519
EP 1055658	A2	20001129	EP 2000-304247	20000519
EP 1055658	A3	20001213		
EP 1055658	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6232476	B1	20010515	US 2000-575310	20000519
AT 234269	E	20030315	AT 2000-304247	20000519
ES 2191597	T3	20030916	ES 2000-304247	20000519
ZA 2000002514	A	20020222	ZA 2000-2514	20000522
IN 188849	A	20021109	IN 2000-MU466	20000522
BR 2000001813	A	20010102	BR 2000-1813	20000523
TR 200001476	A2	20010221	TR 2000-200001476	20000523
RU 2195445	C2	20021227	RU 2000-112848	20000523
AU 769690	B2	20040129	AU 2000-36362	20000523
US 6323345	B1	20011127	US 2001-794382	20010227
US 2002042524	A1	20020411	US 2001-974309	20011009
US 6395911	B2	20020528		
JP 2002205990	A2	20020723	JP 2001-362058	20011128
JP 3600206	B2	20041215		

PRIORITY APPLN. INFO.:	US 1999-135578P	P	19990524
	US 2000-575310	A3	20000519
	JP 2000-152901	A3	20000524
	US 2001-794382	A3	20010227

OTHER SOURCE(S): CASREACT 134:4858; MARPAT 134:4858

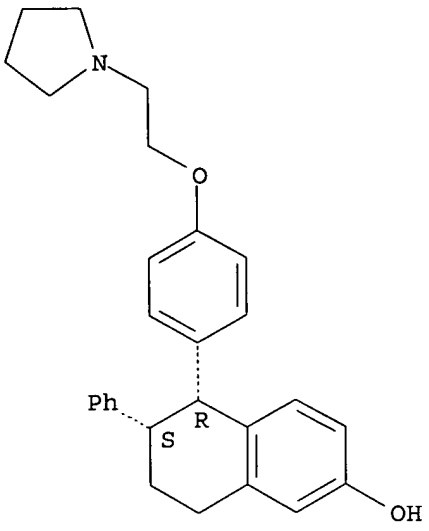
AB The compound is prepared from 2-bromo-5-methoxytoluene via 1-bromo-2-bromomethyl-4-methoxybenzene, 3-(2-bromo-5-methoxyphenyl)-1-phenylpropan-1-one, 2-[2-(2-bromo-5-methoxyphenyl)ethyl]-2-phenyl-[1,3]dioxolane, (4-benzyloxyphenyl)[4-methoxy-2-[2-(2-phenyl[1,3]dioxolan-2-yl)ethyl]phenyl]methanone, 3-[2-(4-benzyloxybenzoyl)-5-methoxyphenyl]-1-phenylpropan-1-one, and 4-(4-benzyloxyphenyl)-7-methoxy-3-phenyl-1,2-dihydronaphthalene.

IT **180916-16-9P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of cis-tetrahydronaphthalene derivative as intermediate for **antiosteoporotic** agent)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:741902 HCAPLUS
DOCUMENT NUMBER: 133:313649
TITLE: Compound preparation made of vitamin D metabolites or vitamin D analogs and an estrogenic component for treating osteoporosis
INVENTOR(S): Knauthe, Rudolf; Erben, Reinhold; Behrens-Stevens, Marie-Luise
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061123	A2	20001019	WO 2000-EP3079	20000406
WO 2000061123	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19916419	A1	20001019	DE 1999-19916419	19990408
DE 19916419	B4	20050616		
EP 1165061	A2	20020102	EP 2000-929342	20000406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541188	T2	20021203	JP 2000-610456	20000406
PRIORITY APPLN. INFO.:			DE 1999-19916419 A	19990408
			WO 2000-EP3079 W	20000406

AB Disclosed is a compound preparation wherein the bone cell activator is a vitamin D metabolite or vitamin D analog and the resorption inhibitor is an estrogenic compound The inventive compound preparation is used in a therapeutical plan which comprises one or more cycles. Each cycle consists of the following steps: a) daily administration of a vitamin D metabolite or vitamin D analog during 1-7 days, b) daily administration of an estrogenic compound during 21-120 days after a) or after an interphase of up to 30 days.

IT **190791-29-8**, Cp336156
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compound preparation made of vitamin D metabolites or vitamin D analogs and an estrogenic component for treating **osteoporosis**)

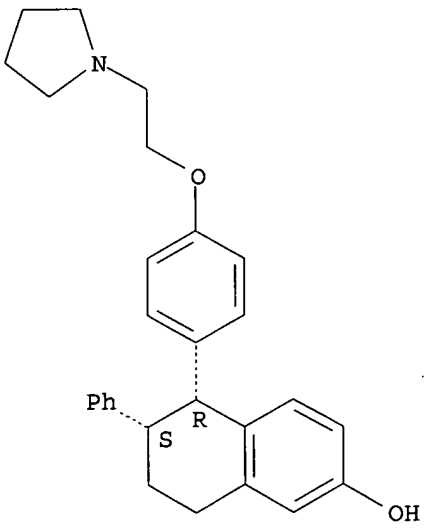
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

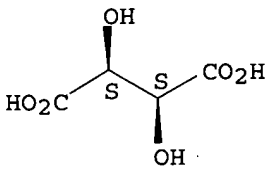
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



L28 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:351207 HCAPLUS
DOCUMENT NUMBER: 132:347946
TITLE: Preparation of dipeptide derivatives as growth hormone secretagogues
INVENTOR(S): Griffith, David Andrew; Bronk, Brian Scott
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

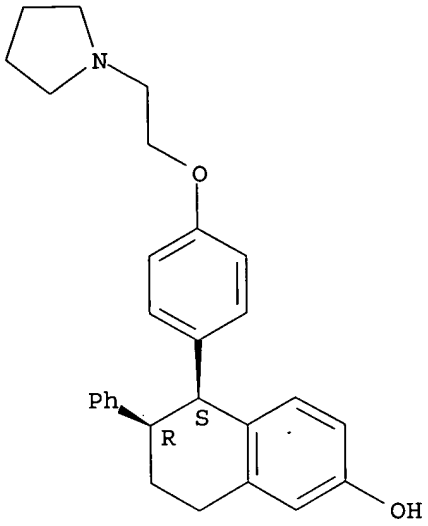
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1002802	A1	20000524	EP 1999-309036	19991112
EP 1002802	B1	20041208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6194578	B1	20010227	US 1999-348449	19990707
AT 284410	E	20041215	AT 1999-309036	19991112
ES 2232088	T3	20050516	ES 1999-309036	19991112
JP 2000159794	A2	20000613	JP 1999-329356	19991119
PRIORITY APPLN. INFO.:			US 1998-109219P P	19981120
OTHER SOURCE(S):	MARPAT 132:347946			

AB Dipeptide derivs. HET-COCR3R4NX4CO-R6-NR7R8 [HET is a heterocyclic moiety; R3 = cycloalkenyl, Ph, heterocyclyl, or bicyclic ring systems (A1), alkyl, A1-alkyl, cycloalkylalkyl, alkoxyalkyl, etc.; R4 = H, alkyl, cycloalkyl or CR3R4 is a ring system; X4 is H, alkyl or X4 and R4 form a ring; R6 is a bond or alkylene which may interrupted by O, S, CH:CH, imino, or a ring; R7, R8 = H, (un)substituted alkyl or R7R8N forms a ring] were prepared as growth hormone secretagogues. Thus, 2-amino-N-[1(R)-benzyloxymethyl-2-[8a(S)-(4-fluorobenzyl)-6-(methylthio)-8-oxo-3,4,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl]-2-oxoethyl]-2-methylpropionamide hydrochloride was prepared via coupling of 8a-(4-fluorobenzyl)-6-(methylthio)-1,3,4,8a-tetrahydro-2H-pyrrolo[1,2-a]pyrazin-8-one hydrochloride with 3(R)-benzyloxy-2-[(2-tert-butoxycarbonylamino)-2-methylpropionylamino]propionic acid. The starting pyrrolopyrazinone derivative was obtained in several steps from 1,2,4-piperazinetricarboxylic acid 1-benzyl 4-tert-Bu 2-Me ester.

IT **180915-78-0P 180915-84-8P 180915-86-0P 180916-14-7P 180916-15-8P 180916-16-9P 193274-89-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dipeptide derivs. as growth hormone secretagogues)

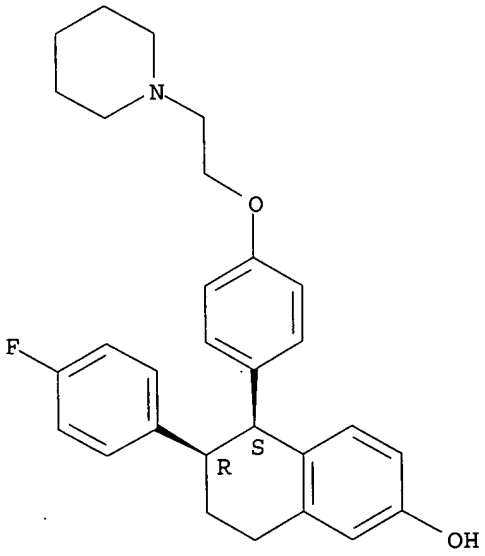
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



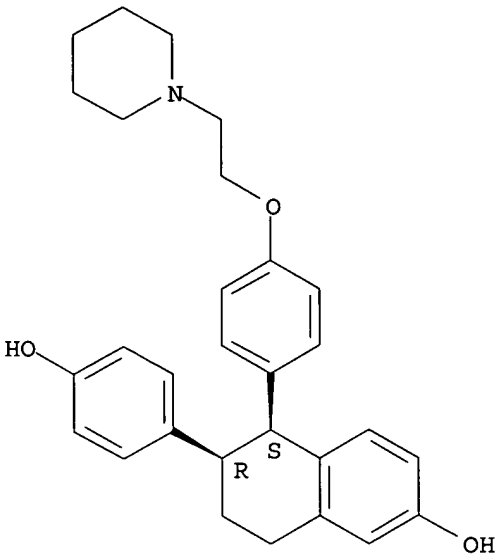
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

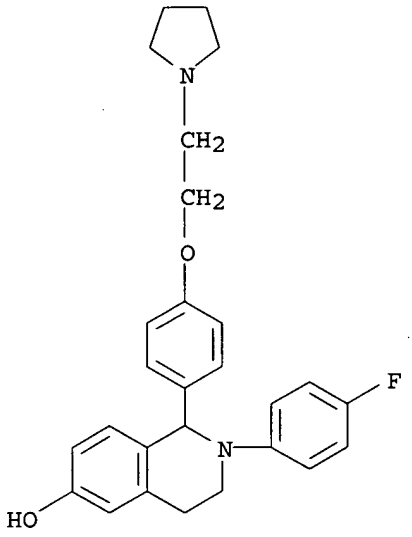


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

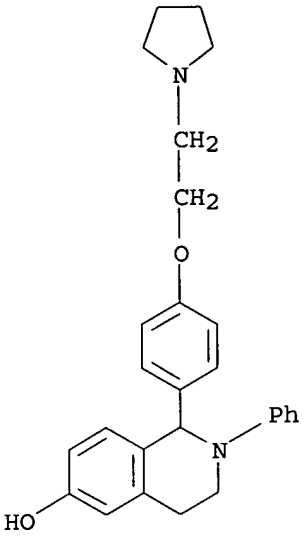
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

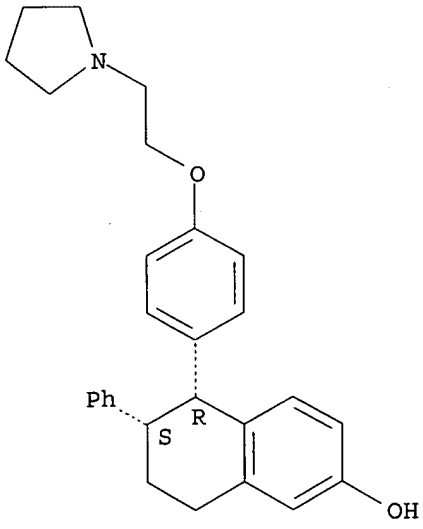


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



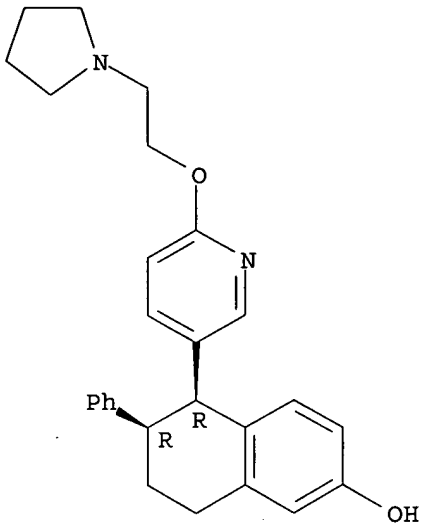
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:257767 HCAPLUS
DOCUMENT NUMBER: 133:26826
TITLE: Lasofoxifene (CP-336,156), a selective estrogen receptor modulator, prevents bone loss induced by aging and orchidectomy in the adult rat
AUTHOR(S): Ke, Hua Zhu; Qi, Hong; Crawford, D. Todd; Chidsey-Frink, Kristin L.; Simmons, Hollis A.; Thompson, David D.
CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases, Central Research Division, Pfizer, Inc., Groton, CT, 06340, USA
SOURCE: Endocrinology (2000), 141(4), 1338-1344
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been well documented that selective estrogen receptor modulators (SERMs) can prevent bone loss in ovariectomized rats and postmenopausal women. The purposes of this study were to determine the effects of a potent and orally active SERM, lasofoxifene (CP-336,156), on bone mass, bone strength, total serum cholesterol, prostate weight, and histol. in adult male orchidectomized (ORX) rats. Sprague Dawley male rats at 10 mo of age were divided into 6 groups, with 10 rats/group. The first group was necropsied on day 0 and served as basal controls. The remaining rats were either sham operated (n = 10) and treated orally with vehicle, or ORX (n = 40) and treated with either vehicle or lasofoxifene at 1, 10, or 100 μg/kg·day for 60 days. Total serum cholesterol, prostate weight and histol., distal femoral bone mineral d. (DFBMD) by dual energy x-ray absorptiometry, and static and dynamic bone histomorphometry of the third lumbar vertebral body were determined Maximal load and stiffness of the fifth lumbar vertebral body were also determined by compression tests. Age-related decreases in DFBMD (-9%) and trabecular bone volume (TBV; -13%) of the third lumbar vertebral body were found in sham-operated rats compared with basal controls. ORX induced significant increases in total serum cholesterol

(+31%), eroded surface (+48%), activation frequency of bone turnover (+103%) and significant decreases in prostate weight (-89%), DFBMD (-14%), TBV (-23%), and maximal load (-17%) compared with basal controls. Compared with sham controls, ORX induced significant increases in eroded perimeter and activation frequency. Lasofoxifene decreased body weight in all dose groups compared with both sham and ORX control values. Compared with ORX controls, ORX rats treated with lasofoxifene at 10 or 100 μg/kg·day had significantly lower percent eroded perimeter activation frequency and significantly higher DFBMD, TBV, and maximal load. Further, lasofoxifene at 10 and 100 μg/kg·day significantly decreased total serum cholesterol by 46% and 68% in ORX rats, whereas no effect was found in prostate weight and histol. parameters compared with ORX control values. These data showed that lasofoxifene prevented bone loss by inhibiting bone turnover associated with aging and orchidectomy in 10-mo-old male rats. Further, lasofoxifene decreased total serum cholesterol and did not affect the prostate in these rats. These results suggest that SERMs such as lasofoxifene may be useful therapeutic agents for preventing bone loss in elderly men with some degree of hypogonadism.

IT **190791-29-8**, CP-336156
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen receptor modulator lasofoxifene prevents bone loss induced by aging and orchidectomy)

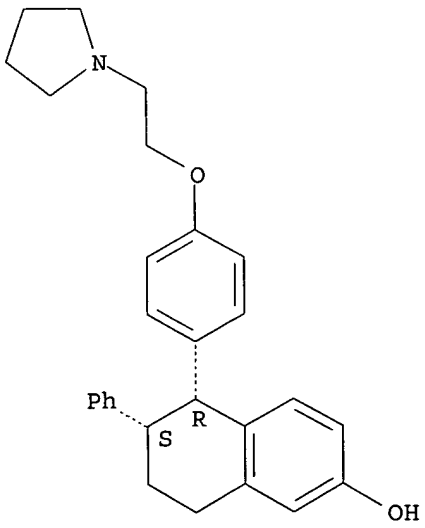
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

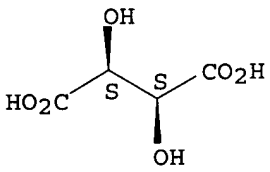
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:151487 HCAPLUS
DOCUMENT NUMBER: 132:203148
TITLE: Heterocycle-containing dipeptide compounds as growth hormone secretagogues, their preparation, compositions containing them, and their applications
INVENTOR(S): Carpino, Philip Albert
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 94 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000072771	A2	20000307	JP 1999-234704	19990820
JP 3486137	B2	20040113		
US 6358951	B1	20020319	US 1999-377326	19990818
CA 2420425	AA	20000221	CA 1999-2420425	19990819
EP 995748	A1	20000426	EP 1999-306576	19990819
EP 995748	B1	20040331		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 263168	E	20040415	AT 1999-306576	19990819
PT 995748	T	20040730	PT 1999-306576	19990819
CA 2280587	C	20040921	CA 1999-2280587	19990819
CA 2280587	AA	20000221		
ES 2217694	T3	20041101	ES 1999-306576	19990819
BR 9903870	A	20001003	BR 1999-3870	19990820
MX 9907844	A	20000331	MX 1999-7844	19990823
US 2002045622	A1	20020418	US 2001-989040	20011121
US 6559150	B2	20030506		
US 2003130284	A1	20030710	US 2002-313495	20021206
US 6686359	B2	20040203		

PRIORITY APPLN. INFO.:

US 1998-97502P	P	19980821
US 1999-377326	A3	19990818
CA 1999-2280587	A3	19990819
US 2001-989040	A3	20011121

OTHER SOURCE(S): MARPAT 132:203148
GI

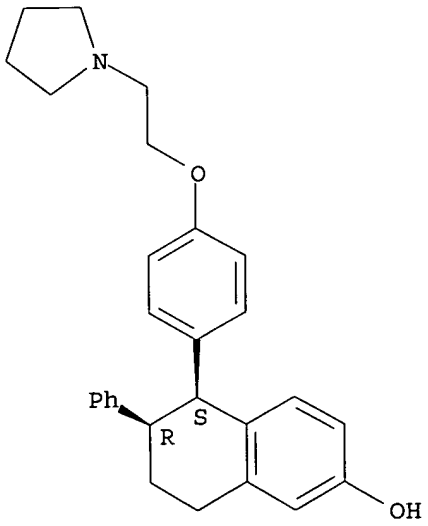
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB HET-COCR3R4NX4COR6NR7R8 [I; HET = heterocyclyl Q, Q1, Q2, Q3, Q4 (definitions for variants are given); R3 = certain (un)substituted ring systems (A1), alkyl, A1-alkyl, etc.; R4 = H, alkyl, cycloalkyl or CR3R4 = a ring system; X4 = H, alkyl, or X4 and R4 form a ring; R6 = linking group containing O, S, CH:CH (hetero)arylene; R7, R8 = H, (un)substituted alkyl or R7R8N forms a ring], mixts. of their stereoisomers, diastereomerically or enantiomerically pure isomers, their pharmaceutically acceptable salts, or their prodrugs are claimed. I are growth hormone secretagogues and are useful for increasing the level of endogenous growth hormone, treating musculoskeletal fragility such as osteoporosis in combination with selective estrogen receptor modulators, treating insulin resistance, enhancing milk production, promoting piglet growth, etc. (preparation given) showed dose-related lowering of plasma glucose and/or insulin levels when administered to female rat of three months, which is consistent with an improvement in glycemic control and insulin sensitivity. The treatment was also associated with trends for decreased plasma lactate, cholesterol, and triglyceride levels, which is also consistent with an improvement in lipid profile and metabolic control as a result of improved insulin sensitivity incurred by this treatment.

IT **180915-78-0 180915-84-8 180916-14-7 180916-15-8 180916-16-9 193274-89-4 260357-98-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulator; preparation of heterocycle-containing amide compds. as growth hormone secretagogues and their applications)

RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

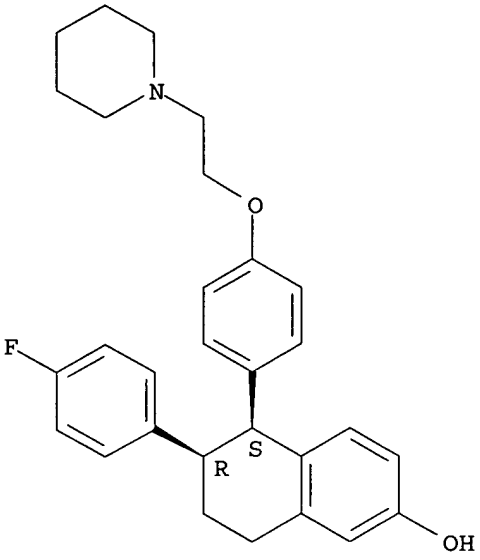
Relative stereochemistry.



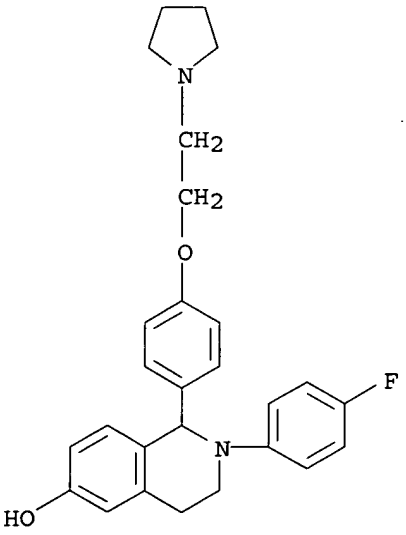
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-

piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

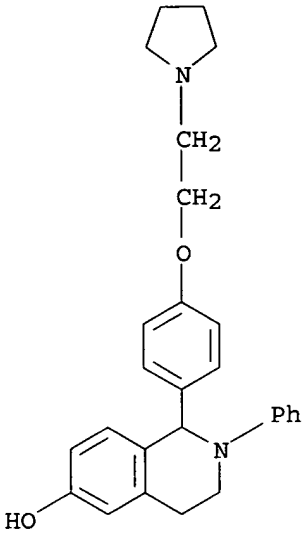
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

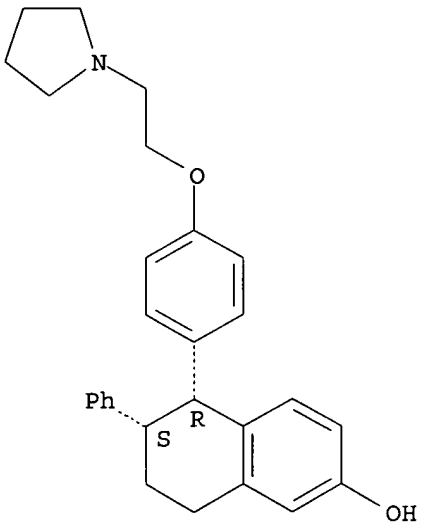


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



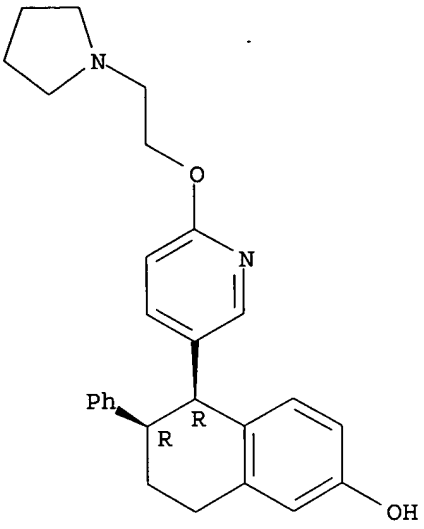
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



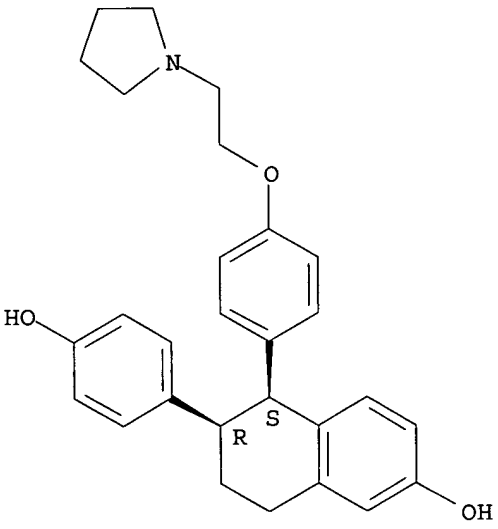
RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 260357-98-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L28 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:116900 HCAPLUS
DOCUMENT NUMBER: 132:156868
TITLE: Use of a NK-1 receptor antagonist for treating or preventing abnormal bone resorption
INVENTOR(S): Hargreaves, Richard John; Rupniak, Nadia Melanie
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000007598	A1	20000217	WO 1999-GB2509		19990730
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2339146	AA	20000217	CA 1999-2339146		19990730
AU 9950599	A1	20000228	AU 1999-50599		19990730
AU 763615	B2	20030731			
EP 1102590	A1	20010530	EP 1999-934993		19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002522389	T2	20020723	JP 2000-563283		19990730
PRIORITY APPLN. INFO.:			GB 1998-16897	A	19980804
			WO 1999-GB2509	W	19990730

OTHER SOURCE(S): MARPAT 132:156868

AB The present invention relates to the use of NK-1 receptor antagonist compns. for the treatment or prevention of abnormal bone resorption, optionally in combination with 1 or more active agents selected from the group consisting of bisphosphonates, estrogen and androgen receptor modulators, and peptide hormones. Thus, tablets contained NK-1 receptor antagonist 50.0, microcryst. cellulose 80.0, modified food corn starch 80.0, lactose 189.5, and Mg stearate 0.5 mg/tablet.

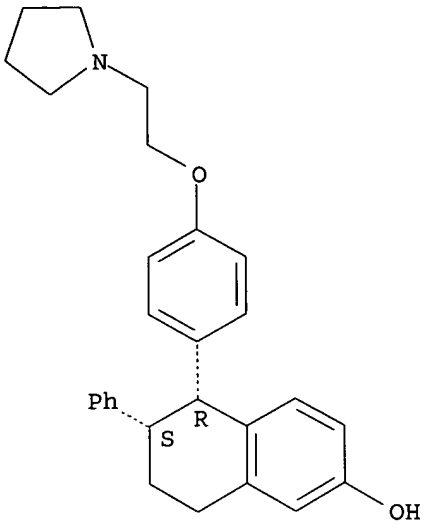
IT **190791-29-8**, CP-336156
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NK-1 receptor antagonist for treatment of or prevention of abnormal bone resorption)

RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

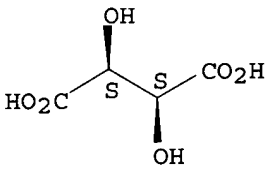
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:672304 HCAPLUS
DOCUMENT NUMBER: 131:295931
TITLE: Treatment of skeletal disorders using leptin or a leptin mimetic
INVENTOR(S): Ke, Hua Zhu; Steppan, Claire Monica; Swick, Andrew Gordon
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 950417	A2	19991020	EP 1999-301084	19990215
EP 950417	A3	20000223		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 6352970	B1	20020305	US 1999-253329	19990219
CA 2262269	C	20030715	CA 1999-2262269	19990219
CA 2262269	AA	19990823		
JP 11315030	A2	19991116	JP 1999-43193	19990222
BR 9900775	A	20000328	BR 1999-775	19990222
US 2002019351	A1	20020214	US 2001-965760	20010927
PRIORITY APPLN. INFO.:			US 1998-75491P	P 19980223
			US 1999-253329	A3 19990219

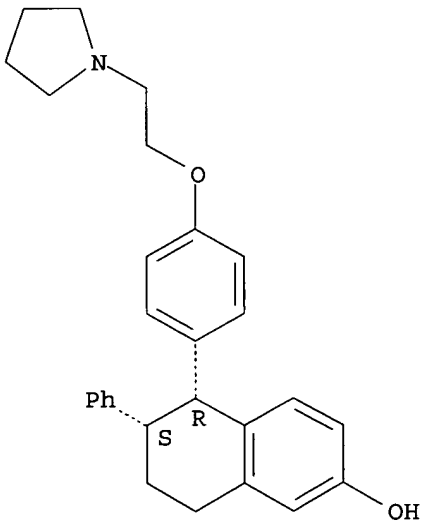
AB This invention relates to methods for treating bone loss in a mammal by administering to the mammal a therapeutically effective amount of leptin or a leptin mimetic. This invention also relates to methods for treating bone fracture, enhancing bone healing following facial reconstruction, maxillary reconstruction or mandibular reconstruction, enhancing long bone extension, enhancing the healing rate of a bone graft, enhancing prosthetic growth and inducing vertebral synostosis by administering a therapeutically effective amount of leptin or a leptin mimetic. This invention further relates to methods and compns. comprising leptin or a leptin mimetic and estrogen, a selective estrogen receptor modulator or a bisphosphonate for treating the above-recited diseases and conditions. Pharmaceutical compns. and kits containing the compds. of the invention are also claimed.

IT **180916-16-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of skeletal disorders using leptin or a leptin mimetic in combination with an estrogen or an estrogen receptor modulator)

RN 180916-16-9 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L28 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:279730 HCAPLUS
DOCUMENT NUMBER: 130:311694

TITLE: Preparation of alkanoic acid and furan-2-carboxylic acid, and thiophene-2-carboxylic acid derivatives for treatment of osteoporosis

INVENTOR(S): Cameron, Kimberly O'Keefe; Lefker, Bruce Allen; Rosati, Robert Louis

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

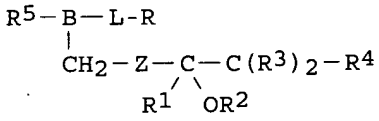
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 911321	A2	19990428	EP 1998-308181	19981008
EP 911321	A3	20010131		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6124314	A	20000926	US 1998-161797	19980928
JP 11180926	A2	19990706	JP 1998-277272	19980930
CA 2249867	AA	19990410	CA 1998-2249867	19981008
BR 9804437	A	20010502	BR 1998-4437	19981009
US 6376502	B1	20020423	US 2000-511128	20000222
US 2002165255	A1	20021107	US 2001-45942	20011019

PRIORITY APPLN. INFO.:

US 1997-61592P	P	19971010
US 1998-161797	A3	19980928
US 2000-511128	A3	20000222

OTHER SOURCE(S): MARPAT 130:311694

GI



I

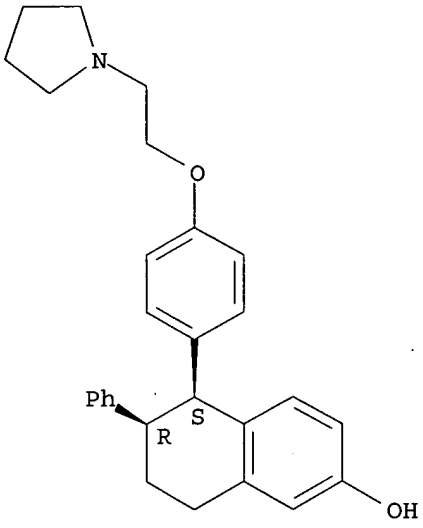
AB The title compds. represented by general formula [I; B = N, CQ1; wherein Q1 = H, C1-3 alkyl; L = n-propylenyl-X- or CH2-m-phenylene-CH2-; wherein X = (un)substituted furanyl, thienyl, thiazolyl, or tetrahydrofuranyl; R = CO2H, C1-6 alkoxycarbonyl, tetrazolyl, 5-oxo-1,2,4-thiadiazolyl, 5-oxo-1,2,4-oxadiazolyl, C1-4 alkylsulfonylcarbamoyl, phenylsulfonylcarbamoyl; R1 = H, Me, Et, n-Pr; R2 = H, C2-5 alkanoyl; R3 = H, F, Me; R4 = H, (un)substituted C1-7 alkyl; or R4 and R1 are taken together to form a 5-9 membered carbocyclic ring; R5 = C1-6 alkylsulfonyl, C3-7 cycloalkylsulfonyl, C3-7 cycloalkyl-C1-6 alkylsulfonyl, C1-6 alkylcarbonyl, C3-7 cycloalkylcarbonyl, C3-7 cycloalkyl-C1-6 alkylcarbonyl, etc.; Z = CH2, CH2CH2, propylene, ethenylene] are prepared This invention relates to prostaglandin agonists, methods of using such prostaglandin agonists, pharmaceutical compns. containing such prostaglandin agonists and kits containing such prostaglandin agonists. The prostaglandin agonists are useful for the treatment of bone disorders including osteoporosis (in particular glucocorticoid-induced osteoporosis, hyperthyroidism-induced osteoporosis, immobilization- induced osteoporosis, heparin-induced osteoporosis or immunosuppressive-induced osteoporosis), osteotomy, childhood idiopathic bone loss or bone loss

associated with periodontitis, for treating kidney regeneration, and for bone healing following facial reconstruction, maxillary reconstruction or mandibular reconstruction (no data). Thus, [3-(methanesulfonylamino-methyl)-phenoxy]-acetic acid Me ester (preparation given) was alkylated by acetic acid 1-(3-chloropropyl)-hexyl ester followed by saponification to give (3-(((4-Hydroxy-nonyl)-methanesulfonyl-amino)-methyl)-phenoxy)-acetic acid.

IT **180915-78-0 180915-84-8 180915-86-0 180916-14-7 180916-15-8 180916-16-9 193274-89-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone antiresorptive agent; preparation of alkanoic acid and furancarboxylic acid, and thiophenecarboxylic acid derivs. for treatment of **osteoporosis**)

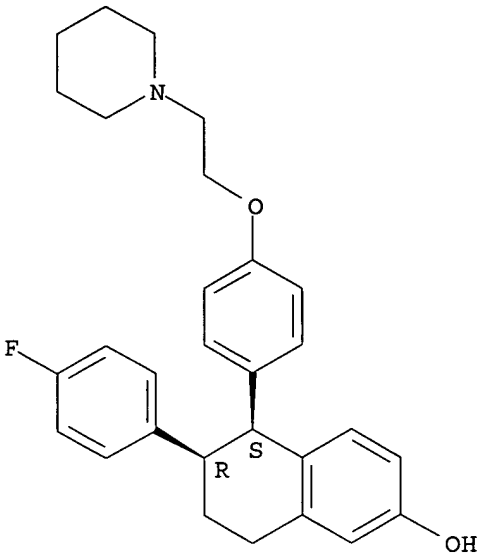
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



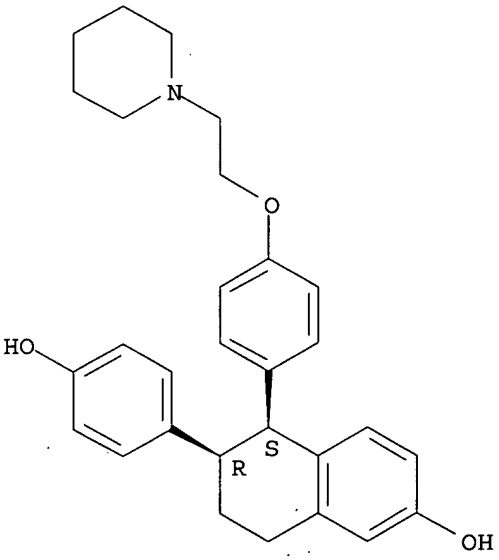
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

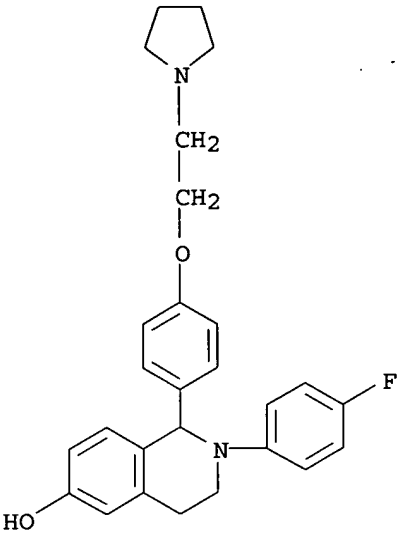


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

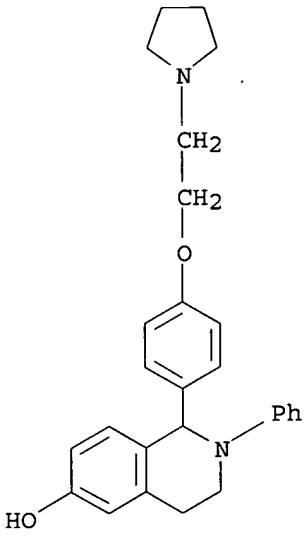
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

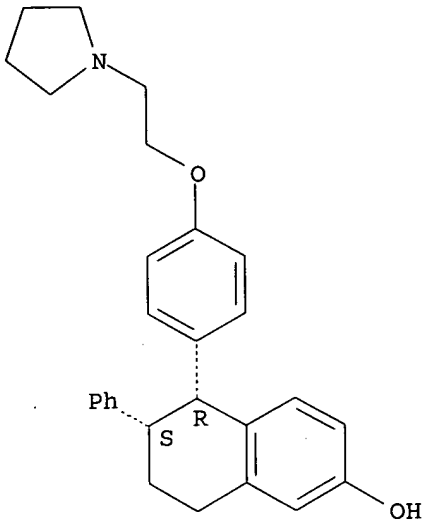


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



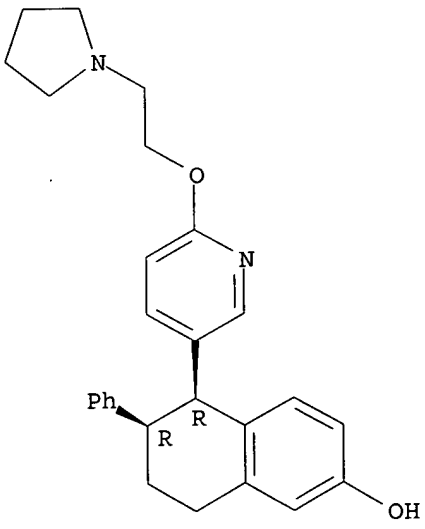
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:271335 HCAPLUS
DOCUMENT NUMBER: 130:311531
TITLE: Preparation of prostaglandin agonists and their use to treat bone disorders
INVENTOR(S): Cameron, Kimberly O'Keefe; Lefker, Bruce Allen; Rosati, Robert Louis
PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: PCT Int. Appl., 255 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919300	A1	19990422	WO 1998-IB1540	19981005
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2305548	AA	19990422	CA 1998-2305548	19981005
AU 9891815	A1	19990503	AU 1998-91815	19981005
AU 731509	B2	20010329		
EP 1021410	A1	20000726	EP 1998-944169	19981005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9813028	A	20000815	BR 1998-13028	19981005
TR 200000927	T2	20001121	TR 2000-200000927	19981005
JP 2001519414	T2	20011023	JP 2000-515873	19981005
JP 3664651	B2	20050629		
TW 570913	B	20040111	TW 1998-87116614	19981007
AP 1156	A	20030630	AP 1998-1356	19981008
W: BW, GM, KE, MW, UG, ZM, ZW				
ZA 9809230	A	20000410	ZA 1998-9230	19981009
US 6498172	B1	20021224	US 1999-367970	19990820
NO 2000001754	A	20000607	NO 2000-1754	20000405
BG 104315	A	20001229	BG 2000-104315	20000407
HR 2000000201	A1	20000630	HR 2000-201	20000410
HR 20000201	B1	20030630		
US 2003078261	A1	20030424	US 2002-256198	20020925
JP 2004155759	A2	20040603	JP 2003-167713	20030612

PRIORITY APPLN. INFO.:

US 1997-61727P	P	19971010
JP 2000-515873	A3	19981005
WO 1998-IB1540	W	19981005
US 1999-367970	A3	19990820

OTHER SOURCE(S): MARPAT 130:311531

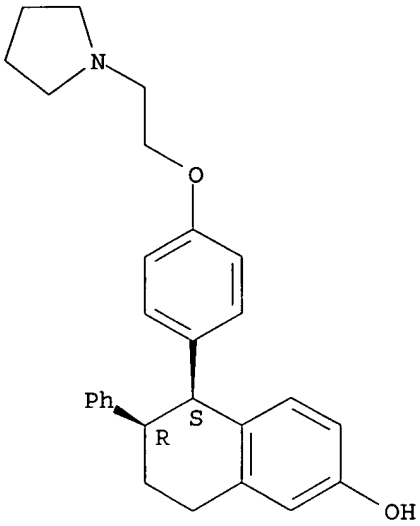
AB Title prostaglandin agonists GAB(KM)QZ [A is SO2, CO; G is Ar, alkylene, ArCONHalkylene, amino, oxyalkylene, etc.; B is N, CH; Q is alkylene, alkyl, alkylene-W-alkylene, alkylene-W-X-alkylene; W is oxy, thio, sulfino, sulfonyl, aminosulfonyl, etc.; X is aryl; K is a bond, alkylene, thioalkylene, alkylenethioalkylene, etc.; M is Ar, ArSar, ArSOAr, ArSO2Ar, ArOAr], prodrugs thereof and the pharmaceutically acceptable salts of said compds. and said prodrugs are prepared as well as methods of using such prostaglandin agonists, pharmaceutical compns. containing such prostaglandin agonists and kits containing such prostaglandin agonists are discussed. The prostaglandin agonists are useful for the treatment of bone disorders including osteoporosis.

IT **180915-78-0 180915-84-8 180915-86-0 180916-14-7 180916-15-8 180916-16-9 193274-89-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(preparation of prostaglandin agonists and their use to treat bone disorders)

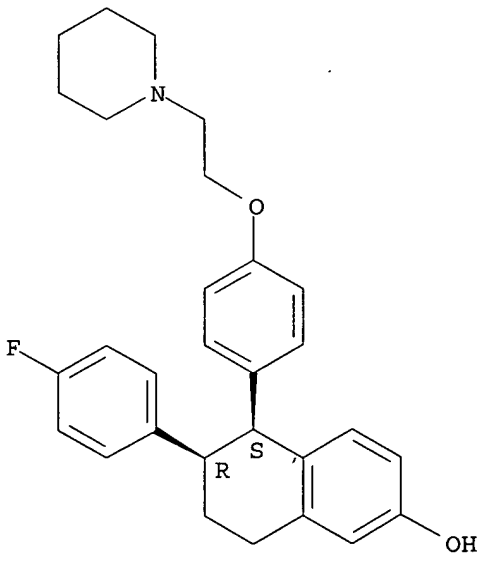
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

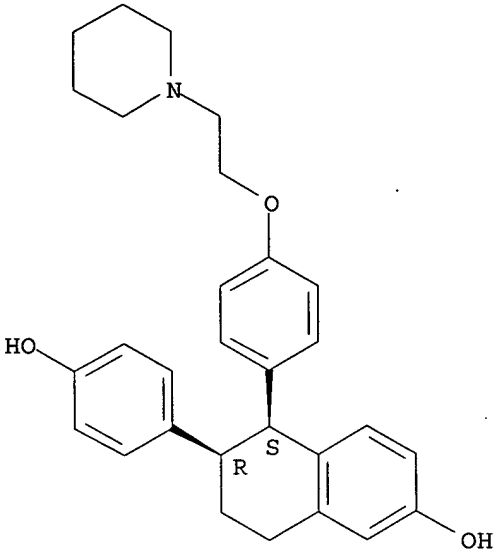
Relative stereochemistry.



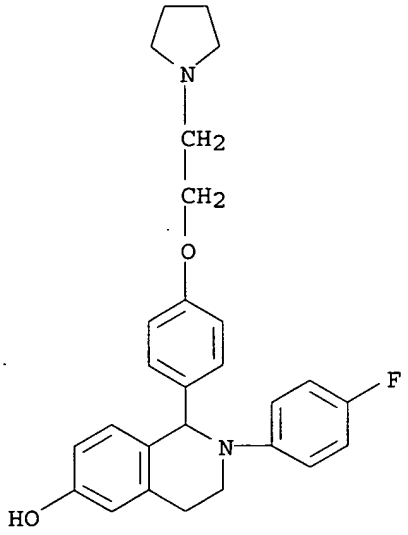
RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-

piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

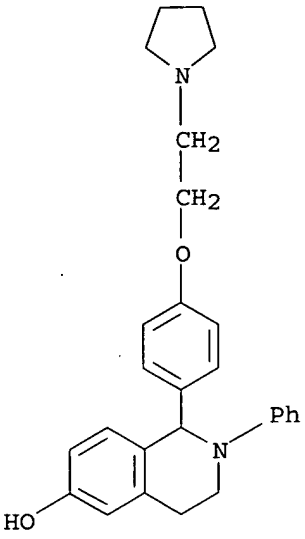
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

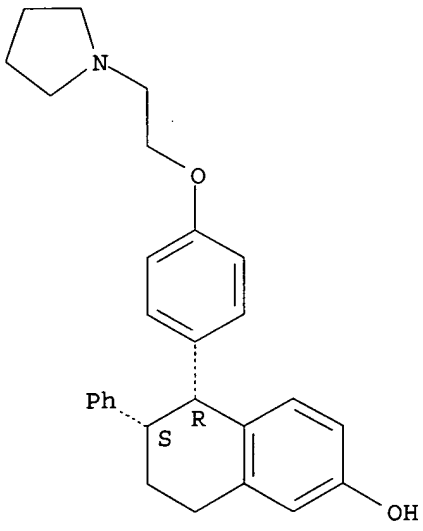


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



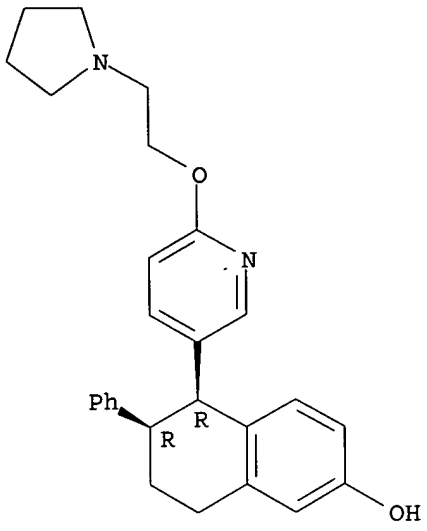
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

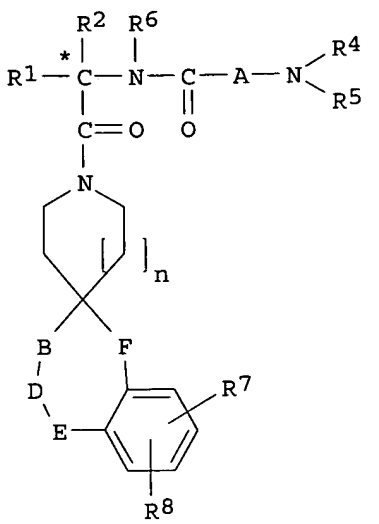


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

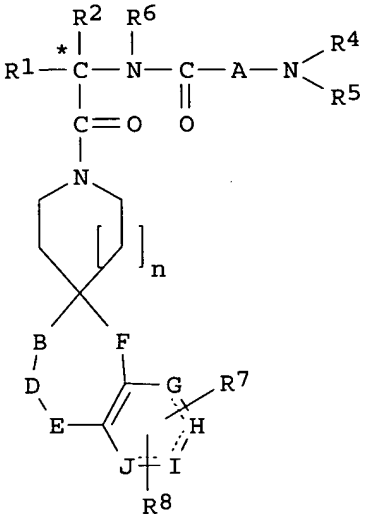
L28 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:109730 HCAPLUS
DOCUMENT NUMBER: 130:148713
TITLE: Combination of growth hormone secretagogues and estrogen receptor modulators for the treatment of osteoporosis
INVENTOR(S): Patchett, Arthur A.; Rodan, Gideon A.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Brit. UK Pat. Appl., 55 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
GB 2324726	A1	19981104	GB 1998-8936		19980427
US 6043026	A	20000328	US 1998-71211		19980501
			US 1997-45290P	P	19970501

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 130:148713
GI



I



II

AB A pharmaceutical composition for the treatment of osteoporosis comprises a combination of a growth hormone secretagogue and an estrogen receptor modulator. The growth hormone secretagogue is of the formula I or II (R1 = alkyl, aryl, arylalkyl, cycloalkyl, etc.; R2 = H, C1-6 alkyl, C3-7 cycloalkyl; R4-R6 = H, C1-6 alkyl; R7,R8 = H, halogen, C1-6 alkyl, cyano, OCF3, methylenedioxy, nitro, etc.; A = alkyl; B,D,E,F = alkyl, O, C=O, S(O)m, etc.; G,H,I,J = C, N, S, O; m = 0-2, n = 1-2) and the pharmaceutically acceptable salts and individual diastereomers thereof. The estrogen receptor modulator is selected from the group consisting of raloxifene, BE 25327, CP 336156, clometherone, delmadinone, droloxifene, idoxifene, nafoxidine, nitromifene, ormeloxifene, tamoxifen, toremifene, trioxifene, and [2-(4-hydroxyphenyl)-6-hydroxynaphthalen-1-yl][4-[2-(1-piperidinyl)-ethoxy]phenyl]methane or pharmaceutically acceptable salts thereof. A 9-wk bone study was conducted in female dogs to evaluate the combined effects of N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H]indole-3,4'-piperidin-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide and raloxifene.

IT **190791-29-8**, CP 336156
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of growth hormone secretagogues and estrogen receptor modulators for treatment of **osteoporosis**)

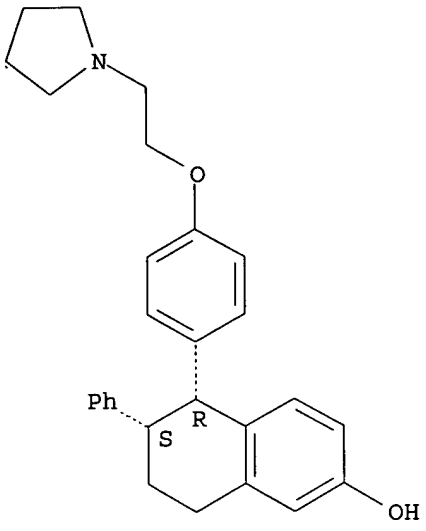
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

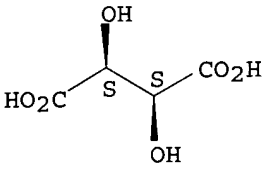
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

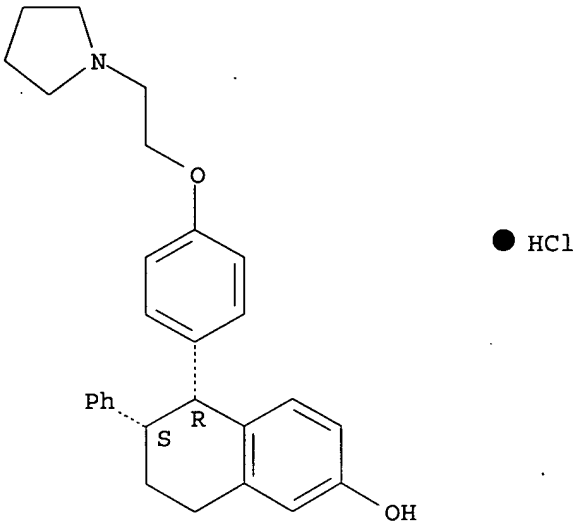
Absolute stereochemistry.



L28 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:33915 HCAPLUS
DOCUMENT NUMBER: 130:191316
TITLE: CP-336156: treatment of osteoporosis
AUTHOR(S): Sorbera, L. A.; Leeson, P. A.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (1998), 23(10), 1066-1070
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 24 refs., of the synthesis, pharmacol., and pharmacokinetics of the title compound, an estrogen receptor modulator.
IT **180915-85-9P 180916-16-9P 190791-29-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(review of CP-336156 for treatment of **osteoporosis**)
RN 180915-85-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, hydrochloride, (5R,6S)- (9CI) (CA INDEX

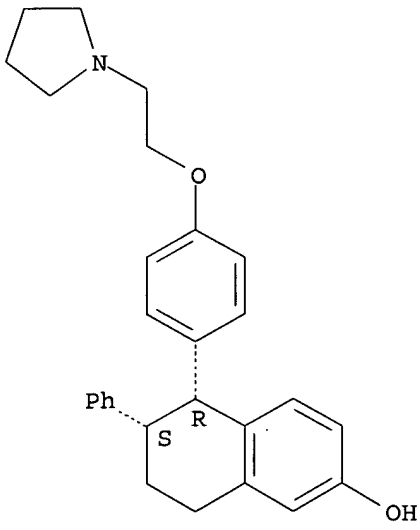
NAME)

Absolute stereochemistry. Rotation (-).



RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



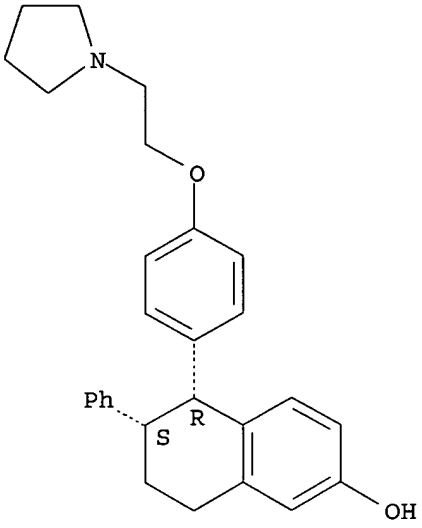
RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9

CMF C28 H31 N O2

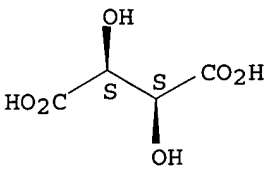
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:27846 HCAPLUS
DOCUMENT NUMBER: 130:66812
TITLE: Tartrate salt of a substituted dipeptide as growth hormone secretagogue
INVENTOR(S): Carpino, Philip Albert; Dasilva-Jardine, Paul Andrew; Lefker, Bruce Allen; Murry, Jerry Anthony
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9858948	A1	19981230	WO 1998-IB874	19980605
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874455	A1	19990104	AU 1998-74455	19980605
AU 744775	B2	20020307		
EP 989993	A1	20000405	EP 1998-921681	19980605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9810623	A	20000725	BR 1998-10623	19980605
TR 9903261	T2	20000821	TR 1999-9903261	19980605
JP 2000514840	T2	20001107	JP 1999-504027	19980605
JP 3414759	B2	20030609		
NZ 500658	A	20010831	NZ 1998-500658	19980605
CA 2294422	C	20030722	CA 1998-2294422	19980605
CA 2294422	AA	19981230		
AP 1043	A	20020204	AP 1998-1266	19980618
W: BW, GM, KE, MW, UG, ZM, ZW				
TW 221153	B1	20040921	TW 1998-87110024	19980622
ZA 9805541	A	20000110	ZA 1998-5541	19980625
US 6248717	B1	20010619	US 1999-380886	19990907
MX 9912100	A	20000430	MX 1999-12100	19991217
NO 9906469	A	20000223	NO 1999-6469	19991223
US 2001016570	A1	20010823	US 2000-734269	20001211
US 6596867	B2	20030722		
PRIORITY APPLN. INFO.:			US 1997-50723P P	19970625
			WO 1998-IB874 W	19980605
			US 1999-380886 A3	19990907

OTHER SOURCE(S): MARPAT 130:66812

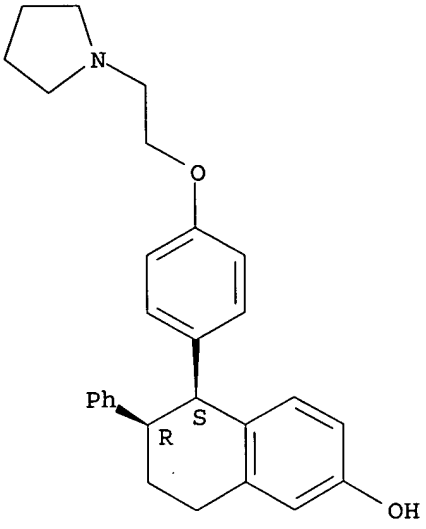
AB Growth hormone secretagogue 2-amino-N-{1-(2,4-difluorobenzyloxymethyl)-2-oxo-2-[3-oxo-3a-pyridin-2-ylmethyl-2-(2,2,2-trifluoroethyl)-2,3,3a,4,6,7-hexahydropyrazolo[4,3-c]pyridin-5-yl]ethyl}-2-methylpropionamide L-tartrate was prepared The synthesis involved reactions of 4-oxopiperidine-1,3-dicarboxylic acid 1-tert-Bu, 3-Et ester, picolyl chloride hydrochloride, CF3CH2NHNH2, N-Boc-D-serine, 2,4-difluorobenzyl bromide, 2-tert-butoxycarbonylamino-2-methylpropionic acid 2,5-dioxopyrrolidin-1-yl ester, and tartaric acid.

IT **180915-78-0 180915-84-8 180915-86-0 180916-14-7 180916-15-8 180916-16-9 193274-89-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of substituted dipeptide tartrate as growth hormone secretagogue)

RN 180915-78-0 HCAPLUS

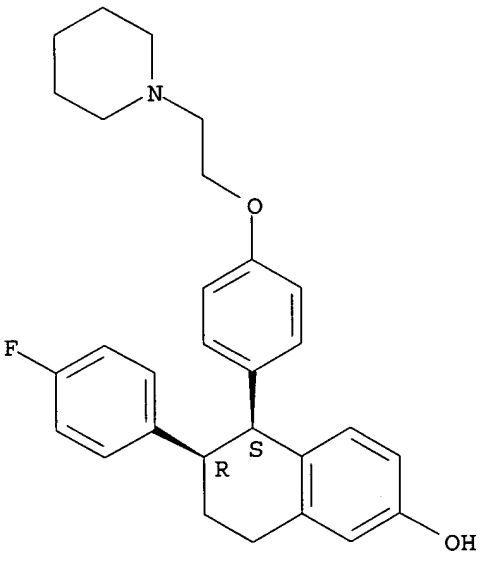
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



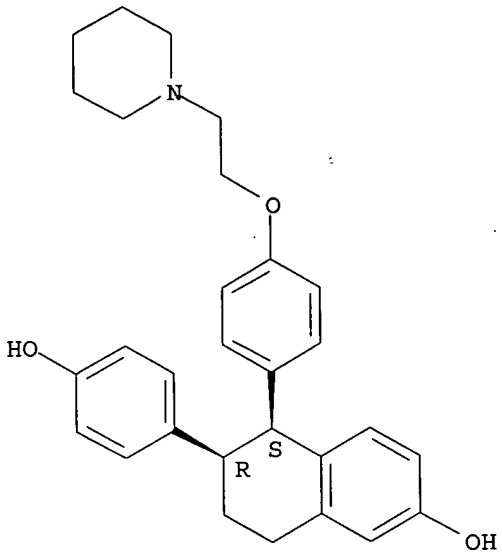
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

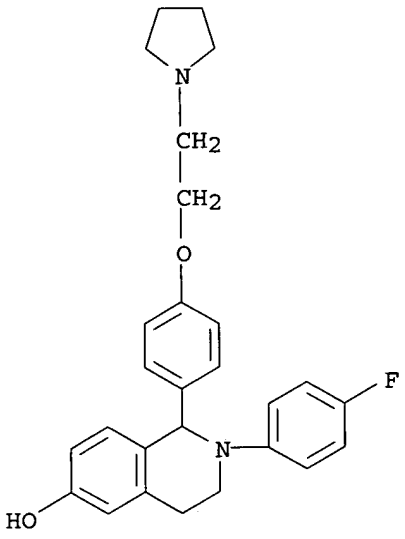


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

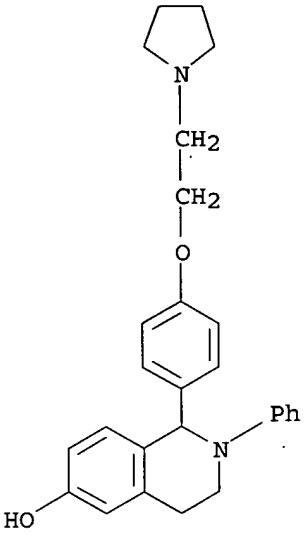
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

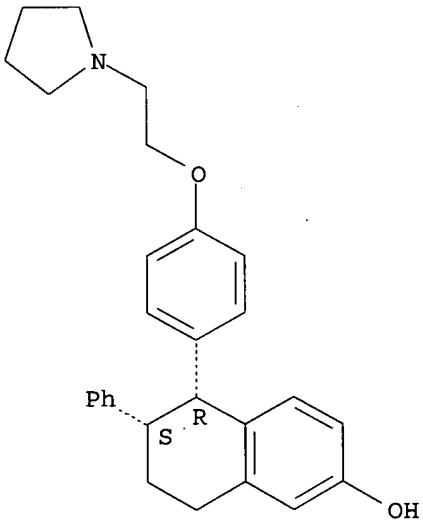


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



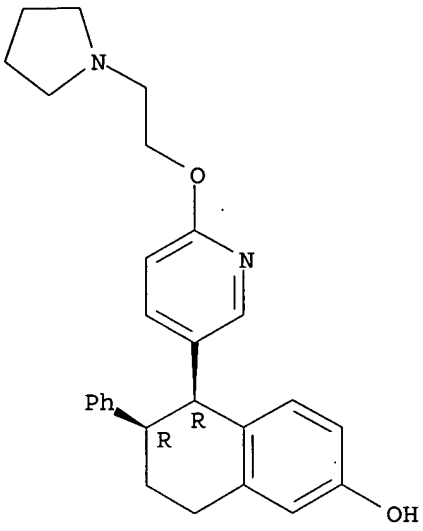
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:27845 HCAPLUS
DOCUMENT NUMBER: 130:95849
TITLE: Dipeptide derivatives as growth hormone secretagogues
INVENTOR(S): Carpino, Philip Albert; Griffith, David Andrew; Lefker, Bruce Allen
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858947	A1	19981230	WO 1998-IB873	19980605
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874454	A1	19990104	AU 1998-74454	19980605
EP 1001970	A1	20000524	EP 1998-921680	19980605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000516639	T2	20001212	JP 1999-504026	19980605
JP 3514774	B2	20040331		
US 6251902	B1	20010626	US 1999-380887	19990908
US 2001041703	A1	20011115	US 2001-822738	20010330
US 6525047	B2	20030225		
US 2002002165	A1	20020103	US 2001-822109	20010330
US 6429313	B2	20020806		

US 2002042415	A1	20020411	US 2001-822095	20010330
US 6432945	B2	20020813		
US 2002065284	A1	20020530	US 2001-823051	20010330
US 6433171	B2	20020813		
US 38524	E	20040601	US 2002-270816	20021015
US 2003216399	A1	20031120	US 2003-371315	20030221
US 2004006063	A1	20040108	US 2003-371330	20030221
US 2004009984	A1	20040115	US 2003-371953	20030221
JP 2004043476	A2	20040212	JP 2003-271589	20030707
JP 3676789	B2	20050727		
JP 2004043477	A2	20040212	JP 2003-271598	20030707
JP 3676791	B2	20050727		
JP 2004067685	A2	20040304	JP 2003-271592	20030707
JP 3676790	B2	20050727		

PRIORITY APPLN. INFO.:

US 1997-50764P	P	19970625
JP 1999-504026	A3	19980605
WO 1998-IB873	W	19980605
US 1999-380887	A3	19990908
US 2001-822738	A3	20010330

OTHER SOURCE(S): MARPAT 130:95849

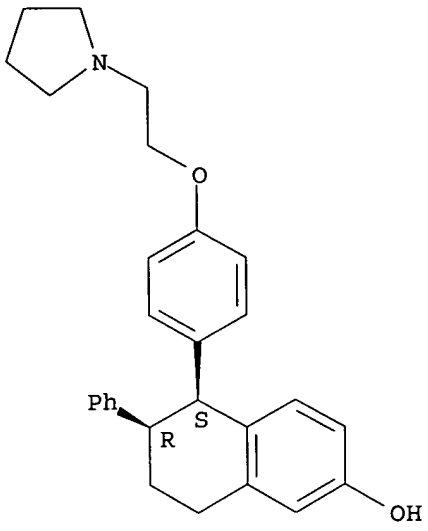
AB Dipeptide derivs. HET-COCR3R4NX4CO-R6-NR7R8 [HET is a heterocyclic moiety; R3 = certain (un)substituted ring systems (A1), alkyl, A1-alkyl, etc.; R4 = H, alkyl, cycloalkyl or CR3R4 is a ring system; X4 is H, alkyl, or X4 and R4 form a ring; R6 is a bond or Z1(CH2)aCX5X5a(CH2)b, where a and b are 0-3, X5 and X5a are H, CF3, A1, (un)substituted alkyl or CX5X5a is a ring or the carbon atom bearing X5 and X5a forms one or two alkylene bridges with the nitrogen atom bearing R7 and R8, Z1 = bond, O, NH or imino group; R7, R8 = H, (un)substituted alkyl or R7R8N forms a ring] were prepared as growth hormone secretagogues. Thus, 2-amino-N-[2-(8a(S)-benzyl-3-oxotetrahydrooxazolo[3,4-a]pyrazin-7-yl)-1(R)-(3,5-dichlorobenzyloxymethyl)-2-oxoethyl]-2-methylpropionamide hydrochloride was prepared from 1,2,4-piperazinetricarboxylic acid 1-benzyl 4-tert-Bu 2-Me ester, N-tert-butoxycarbonyl-α-methylalanine, N-tert-butoxy-D-serine, and 1,3-dichloro-5-chloromethylbenzene.

IT **180915-78-0 180915-84-8 180915-86-0**
180916-14-7 180916-15-8 180916-16-9
193274-89-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of dipeptide derivs. as growth hormone secretagogues)

RN 180915-78-0 HCAPLUS

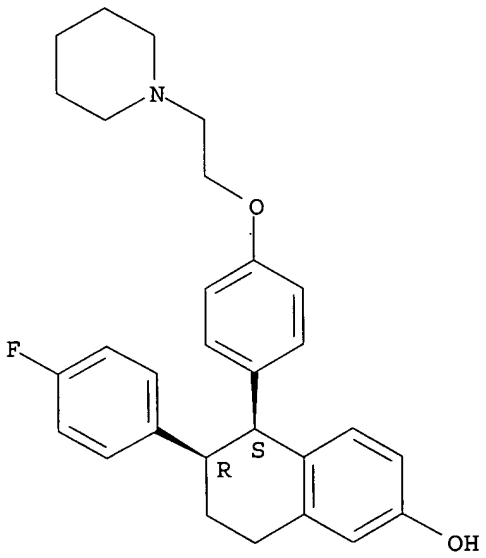
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



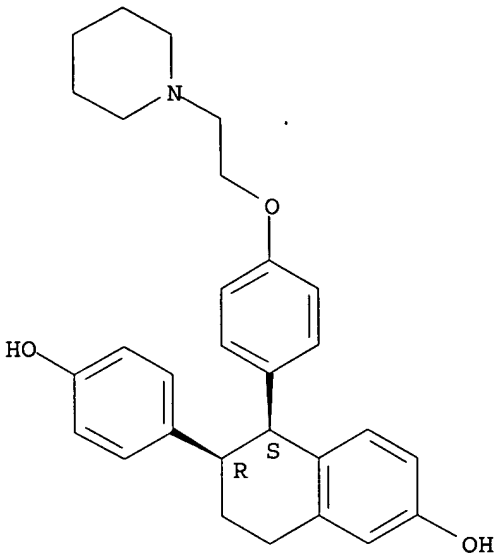
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

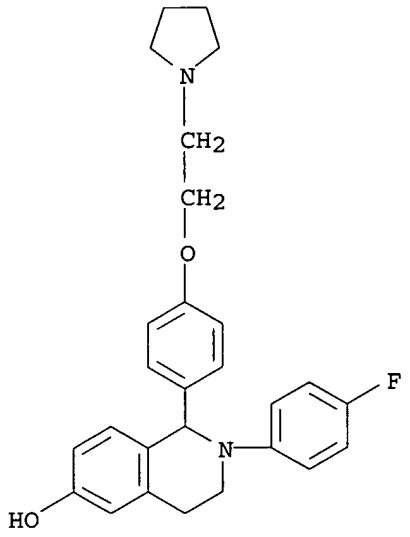


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

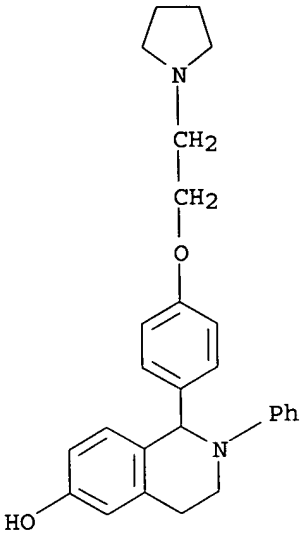
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

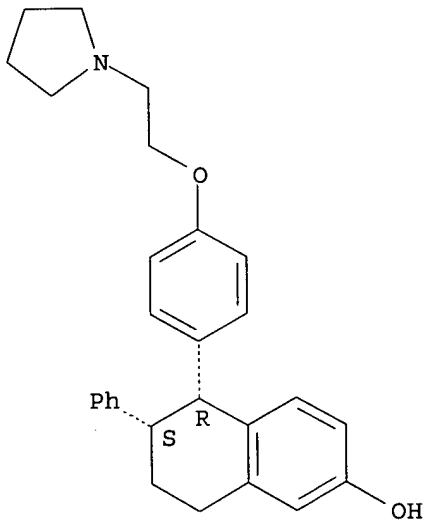


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



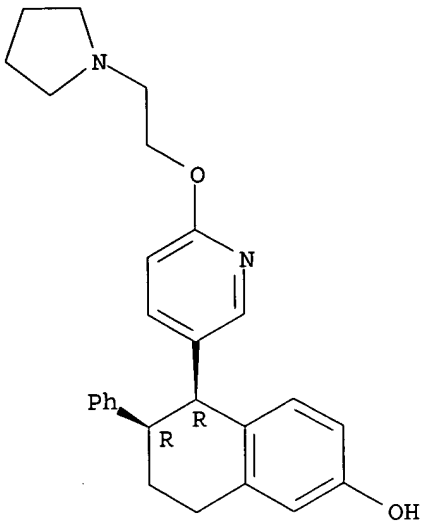
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:344323 HCAPLUS
DOCUMENT NUMBER: 129:23437
TITLE: Estrogen agonists for treating atherosclerosis
INVENTOR(S): Aiello, Robert Joseph
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 842661	A2	19980520	EP 1997-308862	19971105
EP 842661	A3	19980902		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6034102	A	20000307	US 1997-955312	19971021
AT 202702	E	20010715	AT 1997-308862	19971105
ES 2158452	T3	20010901	ES 1997-308862	19971105
IL 122123	A1	20010724	IL 1997-122123	19971106
CA 2221114	AA	19980515	CA 1997-2221114	19971113
CA 2221114	C	20031028		
NZ 329174	A	20001027	NZ 1997-329174	19971113
ZA 9710292	A	19990517	ZA 1997-10292	19971114
AU 9745237	A1	19980521	AU 1997-45237	19971117
AU 740378	B2	20011101		
JP 10147527	A2	19980602	JP 1997-315227	19971117
JP 3287793	B2	20020604		
GR 3036455	T3	20011130	GR 2001-401305	20010827
PRIORITY APPLN. INFO.:			US 1996-31273P P	19961115

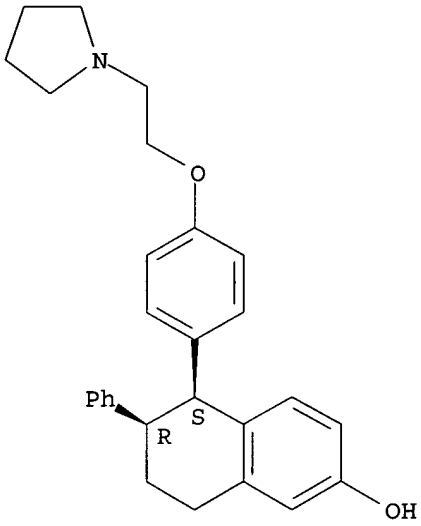
OTHER SOURCE(S): MARPAT 129:23437
AB This invention is directed to a method of treating atherosclerosis,

independent of lipid lowering by inhibiting progression of an atherogenic lesion or by stabilizing plaque. Preferably, such lesion progression inhibition or plaque stabilization is achieved by directly inhibiting chemokine expression leading to excessive inflammatory cell recruitment by administering a compound, such as cis-6-(4-fluorophenyl)-5-[4-(2-piperidin-1-yl-ethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol and (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol.

IT **180915-78-0 180915-84-8 180915-86-0**
180916-14-7 180916-15-8 180916-16-9
193274-89-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonists for treating **atherosclerosis**)

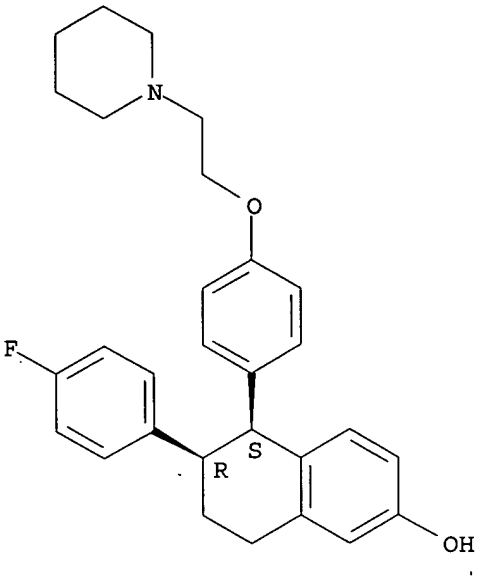
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



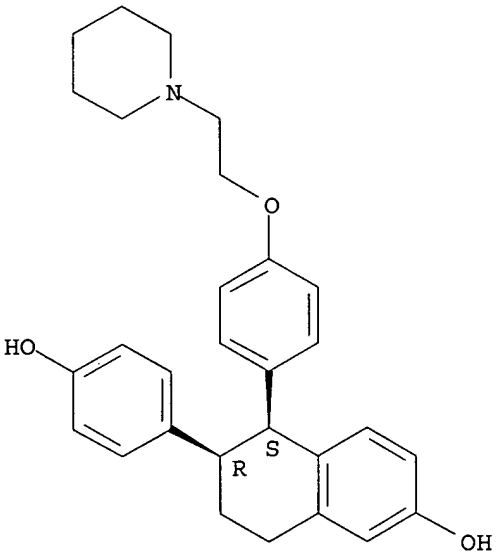
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

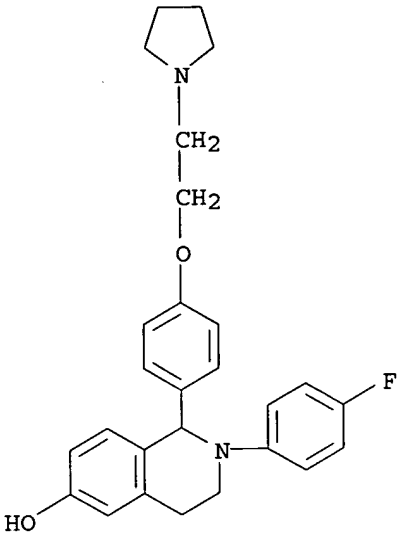


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

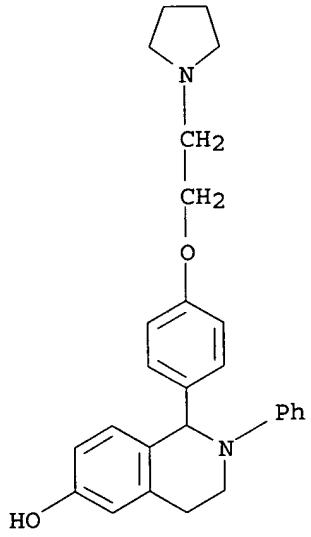
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

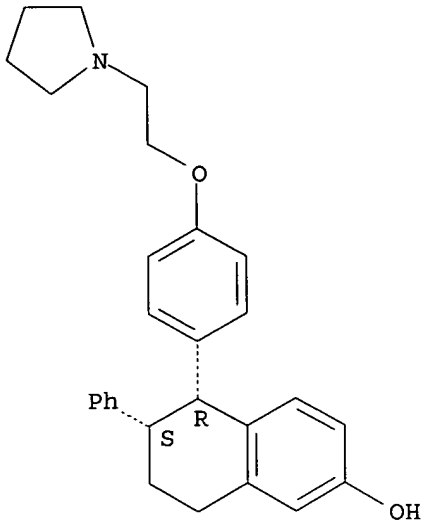


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



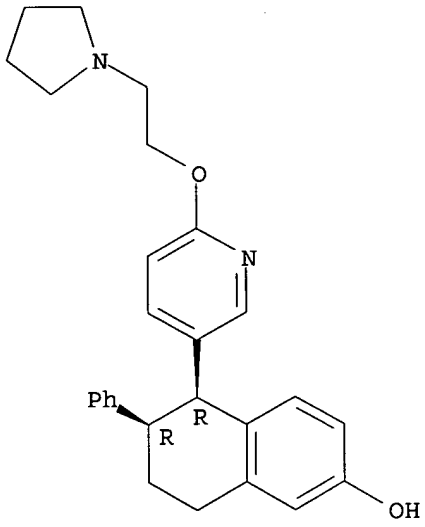
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L28 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:206686 HCAPLUS
DOCUMENT NUMBER: 128:317131
TITLE: Effects of CP-336,156, a new, nonsteroidal estrogen agonist/antagonist, on bone, serum cholesterol, uterus, and body composition in rat models
AUTHOR(S): Ke, Hua Zhu; Paralkar, Vishwas M.; Grasser, William A.; Crawford, D. Todd; Qi, Hong; Simmons, Hollis A.; Pirie, Christine M.; Chidsey-Frink, Kristin L.; Owen, Thomas A.; Smock, Steven L.; Chen, Hong Ka; Jee,

Webster S. S.; Cameron, Kimberly O.; Rosati, Robert L.; Brown, Thomas A.; Dasilva-Jardine, Paul; Thompson, David D.
CORPORATE SOURCE: Central Research Division, Departments of Cardiovascular and Metabolic Diseases, Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Endocrinology (1998), 139(4), 2068-2076
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have discovered a new, nonsteroidal, potent estrogen agonist/antagonist, CP-336,156. CP-336,156 binds selectively and with high affinity to the human estrogen receptor-α with a half-inhibition concentration of 1.5 nM, which is similar to that seen with estradiol (4.8 nM). When given orally to immature (3-wk-old) female Sprague-Dawley rats for 3 days at doses of 0.1, 1.0, 10, or 100 μg/kg/day, unlike 17α-ethynylestradiol, CP-336,156 had no effect on uterine wet or dry weight Similarly, no uterine hypertrophy was observed in aged (17-mo-old) female rats treated (po) with CP-336,156 at 10 or 100 μg/kg/day for 28 days. The authors also found that CP-336,156 decreased total serum cholesterol and fat body mass and had no effect on lean body mass in these aged female rats. In 5-mo-old ovariectomized (OVX) Sprague-Dawley female rats, CP-336,156 completely prevented OVX-induced increases in body weight gain, total serum cholesterol, and serum osteocalcin at doses between 10 and 1000 μg/kg/day after 4 wk. At these doses, CP-336,156 completely prevented OVX-induced bone loss and inhibited the increased bone turnover associated with estrogen deficiency in lumbar vertebrae, proximal tibiae, and distal femora. Similar to estrogen, CP-336,156 induced apoptosis and p53 expression with a concomitant decrease in the number of tartrate-resistant acid phosphatase-pos. multinuclear cells in rat bone marrow cell cultures in vitro, suggesting that the induction of apoptosis may be a mechanism for the estrogenic activities of CP-336,156 in bone. In summary, CP-336,156 is a new, orally active, nonsteroidal, potent estrogen agonist/antagonist that has similar effects in bone as estradiol but without the uterine-stimulating effects associated with estradiol in rats.

IT **190791-29-8**, CP 336156
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CP-336,156 nonsteroidal estrogen agonist/antagonist effect on bone, serum cholesterol, uterus, and body composition in rat models)

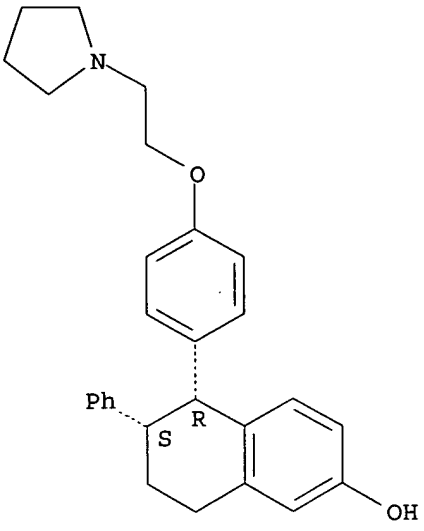
RN 190791-29-8 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

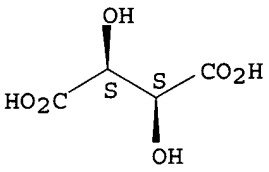
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:600513 HCAPLUS
DOCUMENT NUMBER: 127:253197
TITLE: Combination therapy to treat osteoporosis
INVENTOR(S): MacLean, David B.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 792645	A1	19970903	EP 1997-301174	19970221
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2198534	AA	19970828	CA 1997-2198534	19970226
AU 9714976	A1	19970904	AU 1997-14976	19970227

CN 1165654	A	19971126	CN 1997-103409		19970228
JP 10007562	A2	19980113	JP 1997-45060		19970228
CN 1178668	A	19980415	CN 1997-103412		19970228
PRIORITY APPLN. INFO.:			US 1996-13367P	P	19960228

OTHER SOURCE(S): MARPAT 127:253197

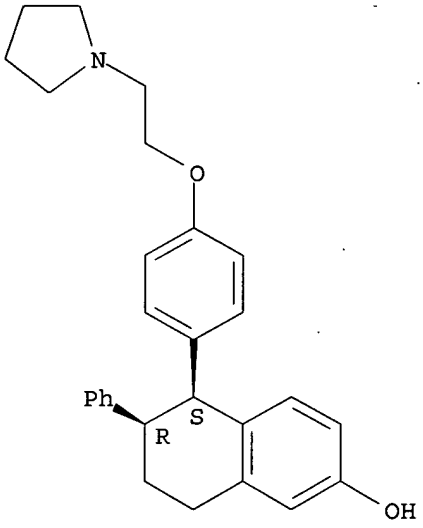
AB A pharmaceutical composition comprising a compound such as cis-6-(4-fluorophenyl)-5-[4-(2-piperidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol in combination with a bone resorption inhibiting polyphosphonate or a progestin is useful for treating or preventing osteoporosis.

IT **180915-78-0 180915-84-8 180915-86-0**
180916-14-7 180916-15-8 180916-16-9
193274-89-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(estrogen agonist in combination with polyphosphonate or progestin in treatment of **osteoporosis**)

RN 180915-78-0 HCAPLUS

CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

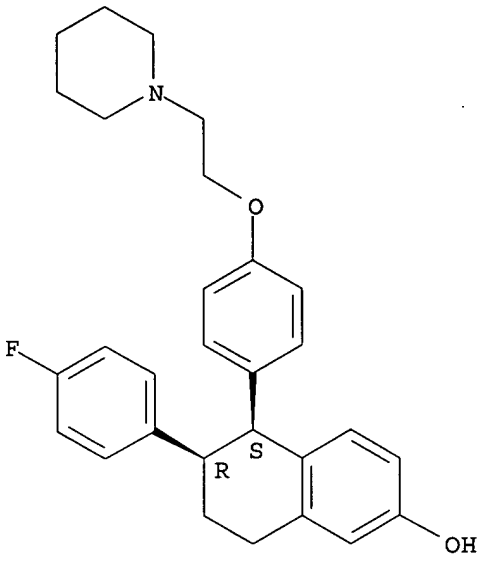
Relative stereochemistry.



RN 180915-84-8 HCAPLUS

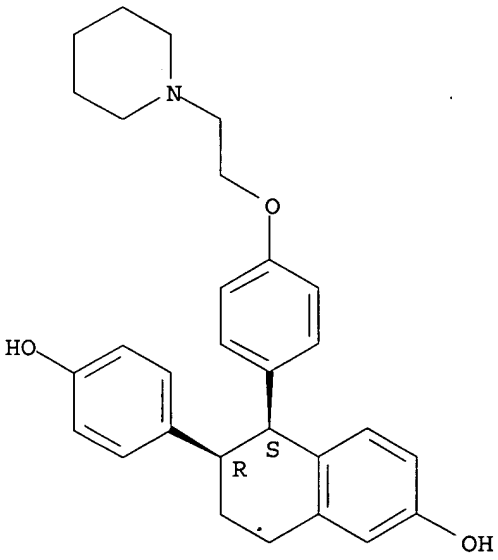
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

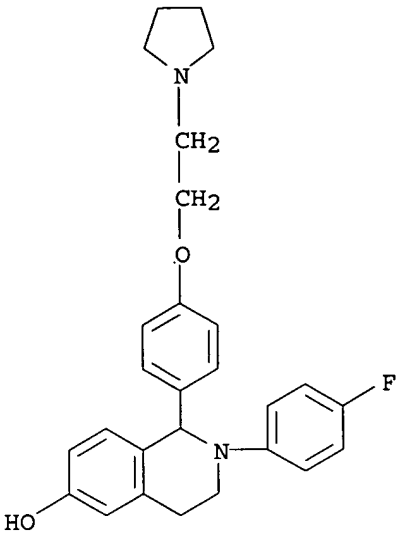


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

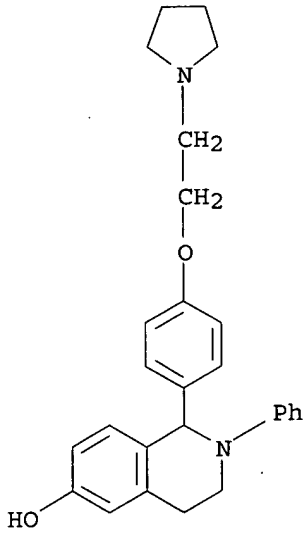
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

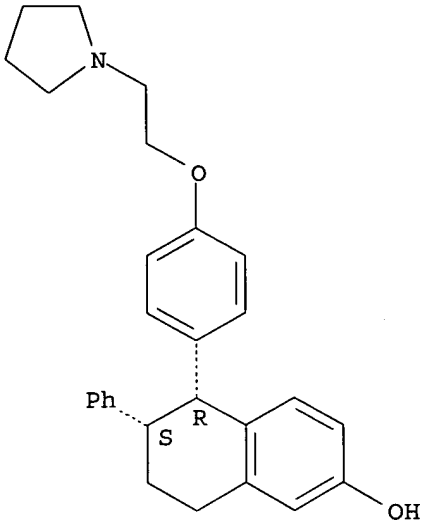


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



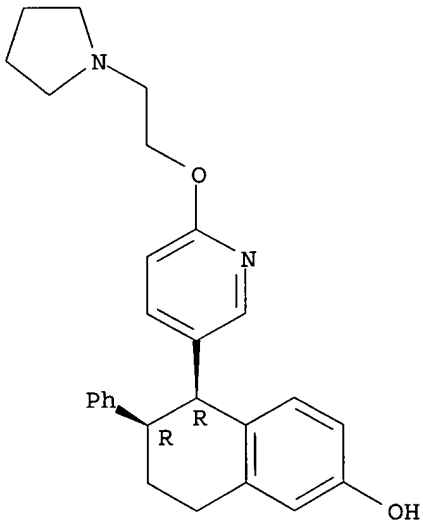
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



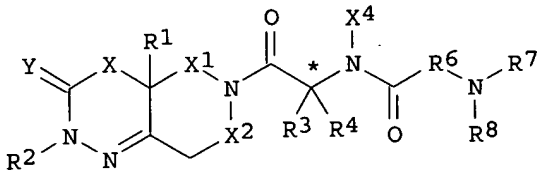
L28 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:547305 HCAPLUS
DOCUMENT NUMBER: 127:149410
TITLE: Preparation of nitrogen heterocyclic peptide analogs as growth-hormone secretagogues
INVENTOR(S): Carpino, Philip A.; Jardine DaSilva, Paul A.; Lefker, Bruce A.; Ragan, John A.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

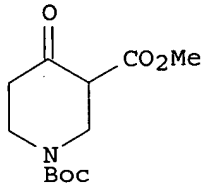
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9724369	A1	19970710	WO 1996-IB1353	19961204
W: AU, BG, BR, BY, CA, CN, CZ, HU, IL, IS, JP, KR, KZ, LK, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 432073	B	20010501	TW 1996-85113857	19961113
CA 2241725	AA	19970710	CA 1996-2241725	19961204
CA 2241725	C	20020618		
AU 9675850	A1	19970728	AU 1996-75850	19961204
AU 716934	B2	20000309		
EP 869968	A1	19981014	EP 1996-938434	19961204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI, RO				
CN 1206422	A	19990127	CN 1996-199388	19961204
CN 1113895	B	20030709		
JP 11501945	T2	19990216	JP 1997-524124	19961204
JP 3511382	B2	20040329		
BR 9612465	A	19990713	BR 1996-12465	19961204
JP 2001213800	A2	20010807	JP 2000-386997	19961204
RU 2172742	C2	20010827	RU 1998-112108	19961204
PL 186916	B1	20040331	PL 1996-327634	19961204
CZ 293423	B6	20040414	CZ 1998-1995	19961204
IL 124449	A1	20040601	IL 1996-124449	19961204
ZA 9610858	A	19980623	ZA 1996-10858	19961223
BG 64055	B1	20031128	BG 1998-102533	19980611
NO 9802991	A	19980826	NO 1998-2991	19980626
US 6107306	A	20000822	US 1999-259691	19990301
US 6110932	A	20000829	US 1999-258956	19990301
US 6124264	A	20000926	US 1999-259776	19990301
US 6278000	B1	20010821	US 1999-470668	19991222
US 6306875	B1	20011023	US 2000-593582	20000613
US 6313140	B1	20011106	US 2000-593581	20000613
US 2002049196	A1	20020425	US 2000-734274	20001211
US 6482825	B2	20021119		

PRIORITY APPLN. INFO.:		
US 1995-9469P	P	19951228
JP 1997-524124	A3	19961204
WO 1996-IB1353	W	19961204
US 1998-68566	A3	19980521
US 1999-258956	A1	19990301
US 1999-259691	A1	19990301
US 1999-259776	A3	19990301

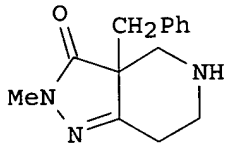
OTHER SOURCE(S): MARPAT 127:149410
GI



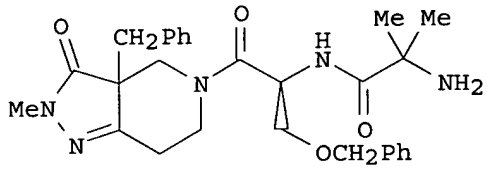
I



II



III



IV

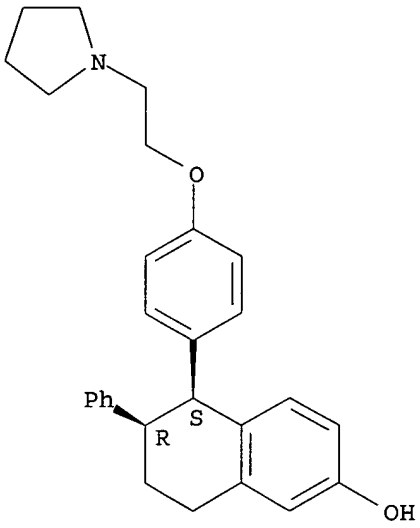
AB Title compds. I [X = CH2, bond; X1, X2 = independently bond, CH2, CH2CH2; Y = O, S; R1 = H, CN, side chain such as (un)substituted (CH2)qN(X6)R, (CH2)tA1, etc.; q = 0-4, t = 0=3; X6 = H, (un)substituted C1-6 alkyl, C3-7 cycloalkyl, etc; A1 = (un)substituted C5-7 cycloalkenyl, Ph, 4-8 membered heterocycle, etc.; R2 = H, (un)substituted C1-8 alkyl, C0-3 alkyl-C3-8 cycloalkyl, C1-4 alkyl-A1; R3 = (un)substituted A1, C1-10 alkyl, C1-6 alkyl-A1, C1-6 alkyl-C3-7 cycloalkyl, etc; R4 = H, (un)substituted C1-6 alkyl, C3-7 cycloalkyl; or R3 and R4 form a ring; X4 = H, C1-6 alkyl; or X4 and R4 form a ring; R6 = bond, Z1(CH2)aC(X5)(X5a)(CH2)b; a = 0-3; b = 0-3; X5, X5a = independently H, CF3, A1, (un)substituted C1-6 alkyl, or form a ring; Z1 = bond, O, NX12, X12 = H, (un)substituted C1-6 alkyl; R7, R8 = independently (un)substituted C1-6 alkyl, or forma a ring] and pharmaceutically-acceptable salts thereof, are growth hormone secretagogues and increase the level of endogenous growth hormone. These compds. are useful for the treatment and prevention of osteoporosis, congestive heart failure, frailty associated with aging, obesity; accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating the recovery of burn patients or patients having undergone major surgery; improving muscle strength, mobility, maintenance of skin thickness, metabolic homeostasis or renal homeostasis. These compds. are also useful in treating osteoporosis when used in combination with: a bisphosphonate compound such as alendronate; estrogen, premarin, and optionally progesterone; an estrogen agonist or antagonist; or calcitonin, and pharmaceutical compns. useful therefor. Further, the present invention is directed to pharmaceutical compns. useful for increasing the endogenous production or release of growth hormone in a human or other animal which comprises an effective amount of a compound of the present invention and a growth hormone secretagogue selected from GHRP-6, Hexarelin, GHRP-1, growth hormone releasing factor (GRF), IGF-1, IGF-2 or B-HT920. The invention is also directed to intermediates useful in the preparation of I. Thus, alkylation of oxopiperidinecarboxylate ester II (Boc = Me3CO2C) (preparation given) with PhCH2Br, followed by cyclocondensation with MeNHNH2

and deprotection gave pyrazolopyridinone III. Amidation of Boc-Aib-D-Ser(CH2Ph)-OH (preparation given) with III, diastereomer separation, and deprotection, gave separated title compds. IV as their HCl salts.

IT **180915-78-0 180915-84-8 180915-86-0 180916-14-7 180916-15-8 180916-16-9 193274-89-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of nitrogen heterocyclic peptide analogs as growth-hormone secretagogues)

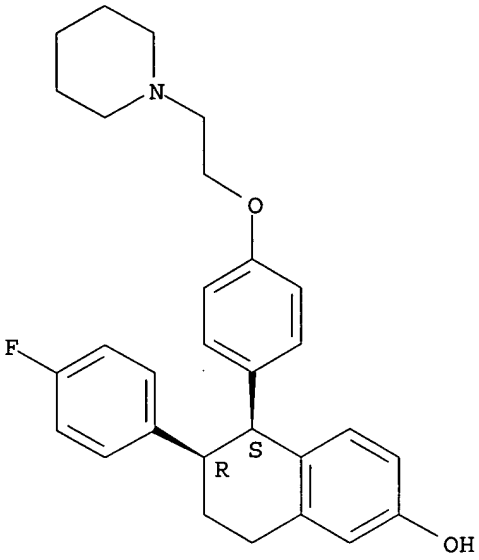
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



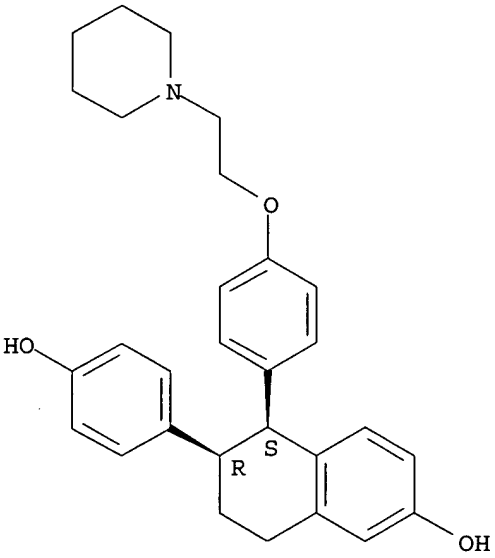
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

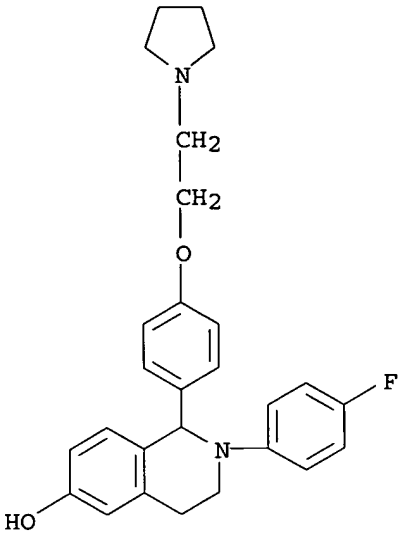


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

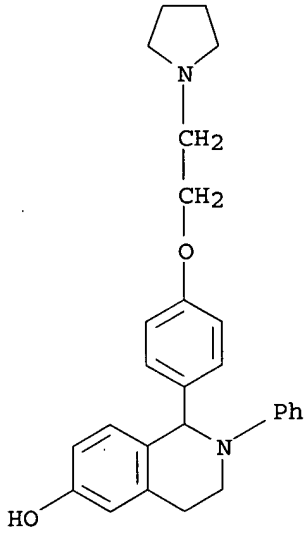
Relative stereochemistry.



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

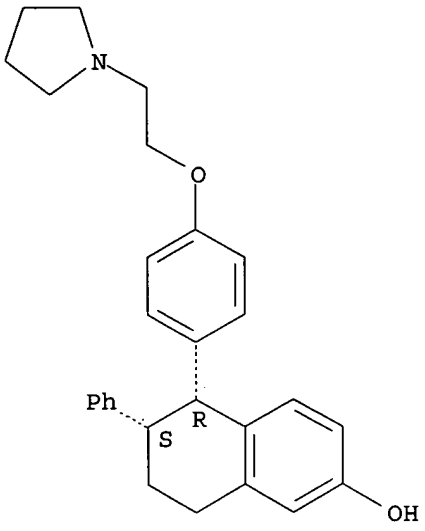


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



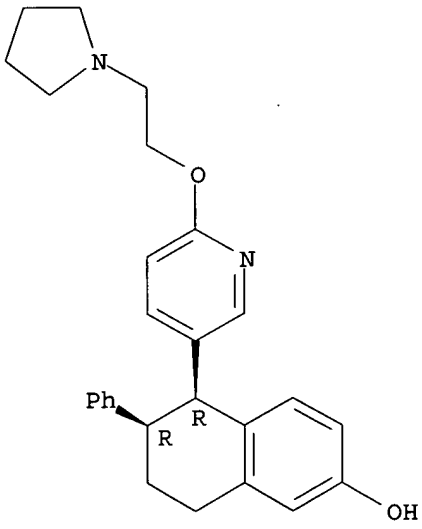
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 193274-89-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



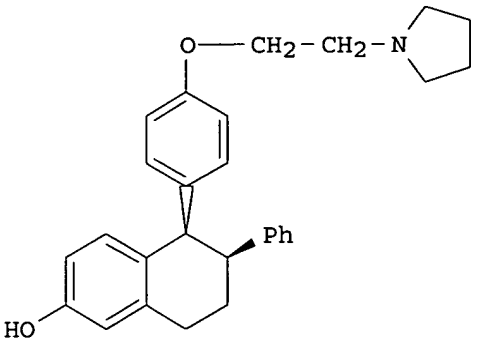
L28 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:414063 HCAPLUS
DOCUMENT NUMBER: 127:34119
TITLE: Preparation of (-)-cis-(5R,6S)-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol D-tartrate by optical resolution
INVENTOR(S): Chiu, Charles K.; Meltz, Morgan
PATENT ASSIGNEE(S): Pfizer Inc., USA; Chiu, Charles K.; Meltz, Morgan
SOURCE: PCT Int. Appl., 16 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716434	A1	19970509	WO 1996-IB1049	19961004
W: AU, BG, BR, BY, CA, CN, CZ, HU, IL, IS, JP, KR, KZ, LK, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 518327	B	20030121	TW 1996-85111903	19960930
TW 581766	B	20040401	TW 2002-91125091	19960930
CA 2236673	AA	19970509	CA 1996-2236673	19961004
CA 2236673	C	20020319		
AU 9669984	A1	19970522	AU 1996-69984	19961004
AU 708841	B2	19990812		
EP 876359	A1	19981111	EP 1996-931206	19961004
EP 876359	B1	20030903		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI				
CN 1201458	A	19981209	CN 1996-198048	19961004
CN 1067065	B	20010613		
JP 11502866	T2	19990309	JP 1997-517180	19961004
JP 3088020	B2	20000918		
BR 9611436	A	19990323	BR 1996-11436	19961004
CZ 287341	B6	20001011	CZ 1998-1320	19961004
RU 2162465	C2	20010127	RU 1998-110128	19961004
IL 124027	A1	20011031	IL 1996-124027	19961004
SK 282172	B6	20011106	SK 1998-542	19961004
AT 248827	E	20030915	AT 1996-931206	19961004
PT 876359	T	20031231	PT 1996-931206	19961004
ES 2203713	T3	20040416	ES 1996-931206	19961004
PL 188633	B1	20050331	PL 1996-326498	19961004
RO 119829	B1	20050429	RO 1998-926	19961004
HR 960503	B1	20011231	HR 1996-960503	19961029
EG 21095	A	20001031	EG 1996-959	19961030
ZA 9609212	A	19980504	ZA 1996-9212	19961101
US 5948809	A	19990907	US 1998-65094	19980428
NO 9801962	A	19980430	NO 1998-1962	19980430
NO 310358	B1	20010625		
BG 63943	B1	20030731	BG 1998-102474	19980521

PRIORITY APPLN. INFO.: US 1995-6125P P 19951102
WO 1996-IB1049 W 19961004

GI



I

AB An advantageous process for the preparation of (-)-cis-(5R,6S)-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalen-2-ol [(5R,6S)-I] D-tartrate involves dissolving racemic or partially optically enriched I in boiling aqueous ethanol to form a solution, adding an equal molar amount of D-tartaric acid in aqueous ethanol to above solution to form a second solution, cooling the second solution, and collecting (5R,6S)-I D-tartrate. A method for treating osteoporosis, cardiovascular disease or hyperlipidemia, prostatic disease, obesity, breast cancer, or endometriosis or for lowering serum cholesterol level in an mammal comprises administering (5R,6S)-I D-tartrate to a mammal. Thus, 1-[2-[4-(2-bromo-6-methoxy-3,4-dihydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine was coupled with phenylboronic acid in the presence of (Ph3P)4Pd and Na2CO3 in THF under reflux for 2 h to give 1-[2-[4-(6-methoxy-2-phenyl-3,4-dihydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine hydrochloride (nafoxidine hydrochloride), which was hydrogenated over Pd(OH)2 in MeOH/EtOH at 50° and 50 psi for 68 h to give cis-1-[2-[4-(6-methoxy-2-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)phenoxy]ethyl]pyrrolidine. This was heated in a mixture of HBr and AcOH at 100° for 15 h followed by treating the hydrobromide salt in CHCl3/MeOH with saturated NaHCO3 solution to give racemic I.

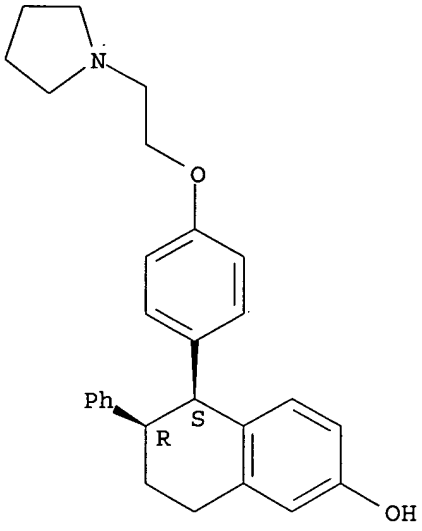
Racemic I (5 g) in a 95:5 mixture of absolute ethanol/H2O (50 mL) was treated with a solution of 1.83 g D-tartaric acid in a 95:5 mixture of absolute ethanol/H2O (20 mL) and heated under gentle reflux to give a homogeneous solution, which was cooled and stirred at ambient temperature (.apprx.25°) overnight. The salt precipitated out as a white solid, collected by suction filtration, washed with 20 mL absolute ethanol, and dried under vacuum to give 2.77 g (5R,6S)-I, which was recrystd. from the same solvent to give 2.48 g (5R,6S)-I with an optical purity of >99.1%. (5R,6S)-I D-tartrate was administered to rats by s.c. injection to decrease prostate weight

IT **180915-78-0P 180915-90-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (-)-cis-(5R,6S)-phenyl[(pyrrolidinylethoxy)phenyl]tetrahydronaphthalen-2-ol D-tartrate by optical resolution for disease treatment)

RN 180915-78-0 HCAPLUS

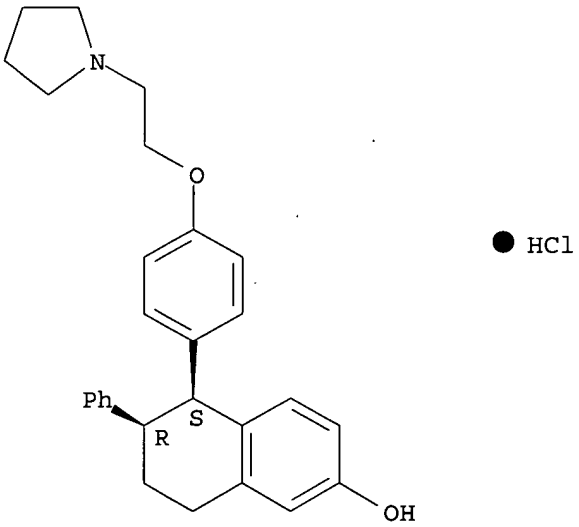
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 180915-90-6 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

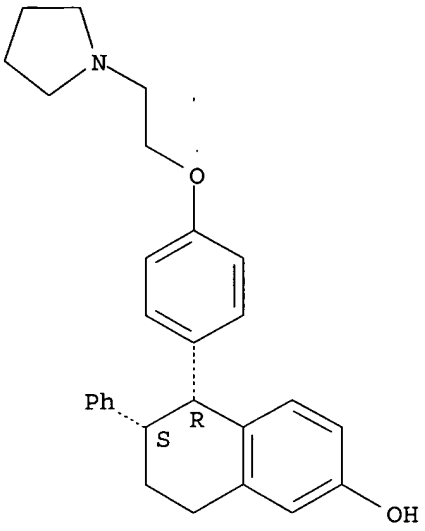


IT **190791-29-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (-)-cis-(5R,6S)-phenyl[(pyrrolidinylethoxy)phenyl]tetrahydronaphthalen-2-ol D-tartrate by optical resolution for disease treatment)
RN 190791-29-8 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 180916-16-9
CMF C28 H31 N O2

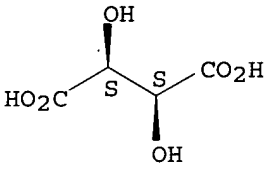
Absolute stereochemistry. Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.



L28 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:551346 HCAPLUS
DOCUMENT NUMBER: 125:195446
TITLE: Preparation of 5-[4-(2-heterocyclylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ols and 1-[4-(2-heterocyclylethoxy)phenyl]-6-hydroxy-1,2,3,4-tetrahydroisoquinolines as estrogen agonists/antagonists
INVENTOR(S): Cameron, Kimberly O.; Jardine, Paul A. DaSilva
PATENT ASSIGNEE(S): Pfizer, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9621656	A1	19960718	WO 1995-IB286	19950424
W: CA, FI, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5552412	A	19960903	US 1995-369954	19950109
CA 2209925	AA	19960718	CA 1995-2209925	19950424
CA 2209925	C	20000801		
EP 802910	A1	19971029	EP 1995-914493	19950424
EP 802910	B1	20020313		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
JP 10503215	T2	19980324	JP 1995-521528	19950424
JP 2972347	B2	19991108		
EP 1151998	A1	20011107	EP 2001-120246	19950424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 214382	E	20020315	AT 1995-914493	19950424
PT 802910	T	20020731	PT 1995-914493	19950424
ES 2172579	T3	20021001	ES 1995-914493	19950424
EP 1411049	A1	20040421	EP 2003-26477	19950424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
SK 281992	B6	20010911	SK 1995-1648	19951222
IL 116643	A1	20000813	IL 1996-116643	19960101
IL 130761	A1	20001206	IL 1996-130761	19960101
RU 2130454	C1	19990520	RU 1996-100074	19960105
NO 9600081	A	19960710	NO 1996-81	19960108
NO 305435	B1	19990531		
CN 1136562	A	19961127	CN 1996-100634	19960108
CN 1059902	B	20001227		
LV 11460	B	19961220	LV 1996-4	19960108
ZA 9600095	A	19970708	ZA 1996-95	19960108
CZ 285085	B6	19990512	CZ 1996-55	19960108
PL 183474	B1	20020628	PL 1996-312182	19960108
AU 9640916	A1	19960718	AU 1996-40916	19960109
AU 700982	B2	19990114		
BR 9600079	A	19980127	BR 1996-79	19960109
HR 960010	B1	20020630	HR 1996-960010	19960109
US 6204286	B1	20010320	US 1997-849726	19970630
FI 9702903	A	19970708	FI 1997-2903	19970708
US 6153622	A	20001128	US 1998-141613	19980828
US 6441193	B1	20020827	US 1999-466034	19991217
US 2001025051	A1	20010927	US 2001-820158	20010328
US 2002132816	A1	20020919	US 2002-147725	20020516

PRIORITY APPLN. INFO.:

US 1995-369954	A1	19950109
EP 1995-914493	A3	19950424
WO 1995-IB286	W	19950424
IL 1996-116643	A3	19960101
US 1997-849726	A1	19970630
US 1999-466034	A1	19991217
EP 2001-120246	A3	20010823

OTHER SOURCE(S): MARPAT 125:195446

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

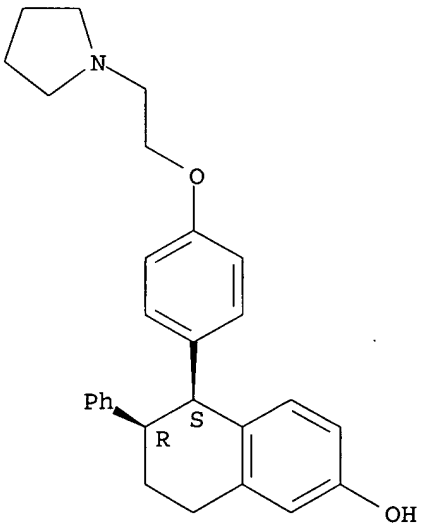
AB The title compds. [I; A = CH2, (substituted) NH; B, D, E = CH, N; Y = (substituted) Ph, naphthyl, C3-8 cycloalkyl, etc.; Z1 = (substituted)

SCH2CH2, OCH2CH2, etc.; G = (substituted) NH2, pyrrolidino, piperidino, etc.; e = 0-2], useful for treating or preventing obesity, breast cancer, osteoporosis, endometriosis, cardiovascular disease, hypercholesterolemia and prostatic disease, were prepared Thus, hydrogenation of nafoxidene.HCl (II.HCl) over palladium hydroxide/C in EtOH followed by treatment of the intermediate cis-III with BBr3/CH2Cl2 afforded cis-I [A = CH2; B, D, E = CH; Y = Ph; Z1 = OCH2CH2; G = pyrrolidino; e = 1; 2-OH]. Compds. I significantly (P < 0.05) decreased prostate weight compared to control in male Sprague-Dawley rats.

IT **180915-78-0P 180915-79-1P 180915-80-4P**
180915-81-5P 180915-82-6P 180915-83-7P
180915-84-8P 180915-85-9P 180915-86-0P
180915-87-1P 180915-88-2P 180915-89-3P
180915-90-6P 180915-91-7P 180915-92-8P
180915-93-9P 180916-14-7P 180916-15-8P
180916-16-9P 181137-16-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 5-[4-(2-heterocyclylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ols and 1-[4-(2-heterocyclylethoxy)phenyl]-6-hydroxy-1,2,3,4-tetrahydroisoquinolines as estrogen agonists/antagonists)

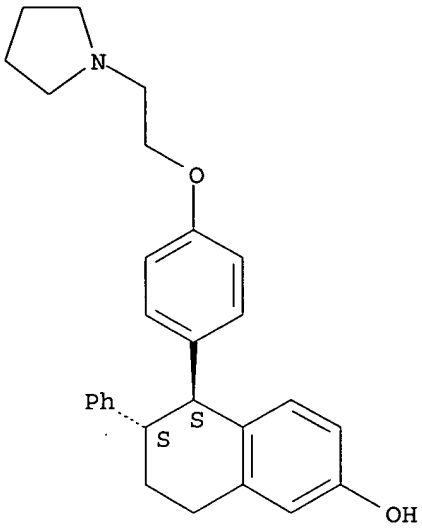
RN 180915-78-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

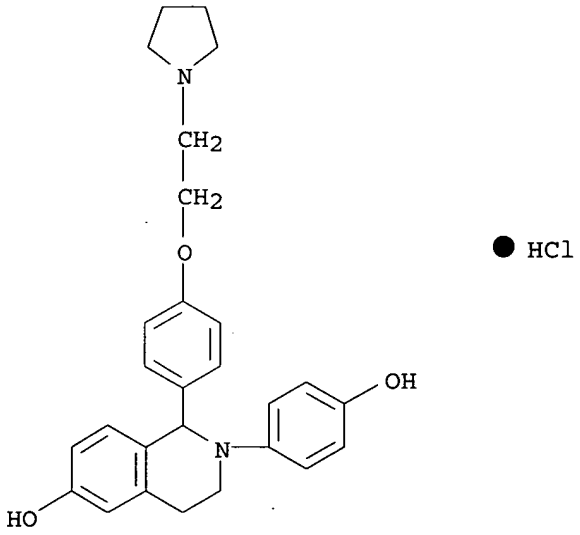


RN 180915-79-1 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

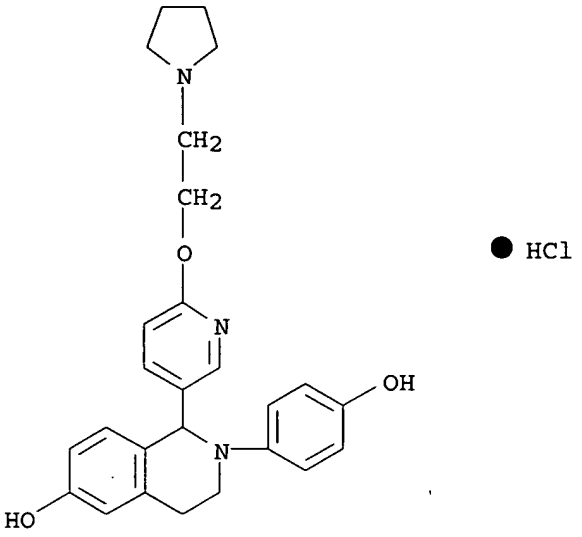
Relative stereochemistry.



RN 180915-80-4 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

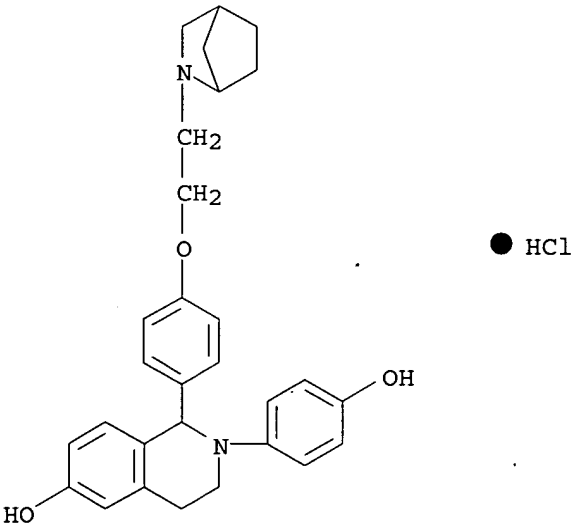


RN 180915-81-5 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)-1-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

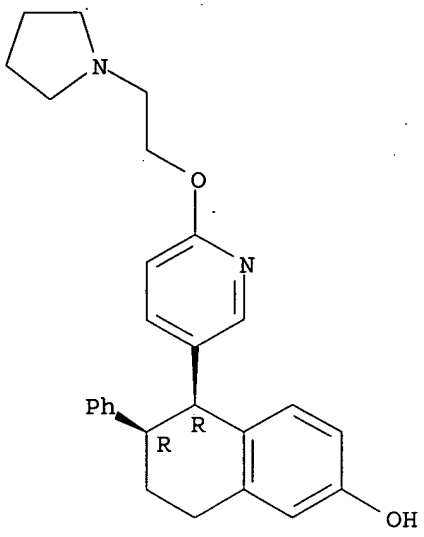
RN 180915-82-6 HCAPLUS
CN 6-Isoquinolinol, 1-[4-[2-(2-azabicyclo[2.2.1]hept-2-yl)ethoxy]phenyl]-1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

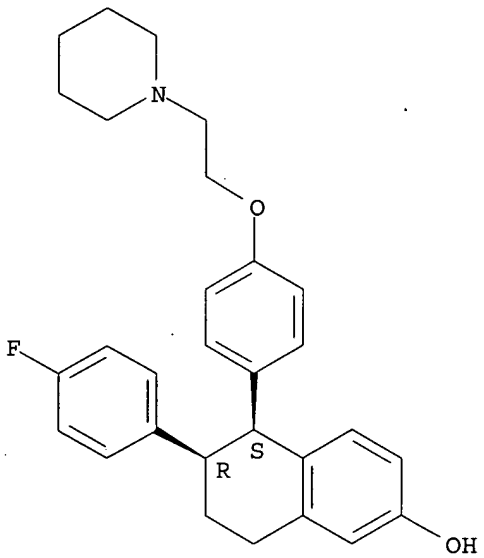
RN 180915-83-7 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



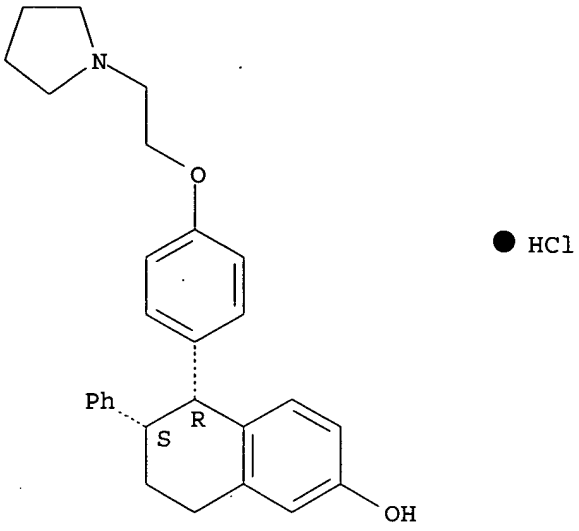
RN 180915-84-8 HCAPLUS
CN 2-Naphthalenol, 6-(4-fluorophenyl)-5,6,7,8-tetrahydro-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



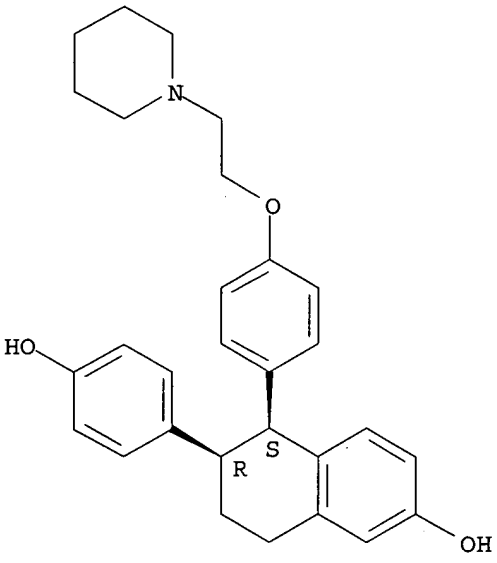
RN 180915-85-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, hydrochloride, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

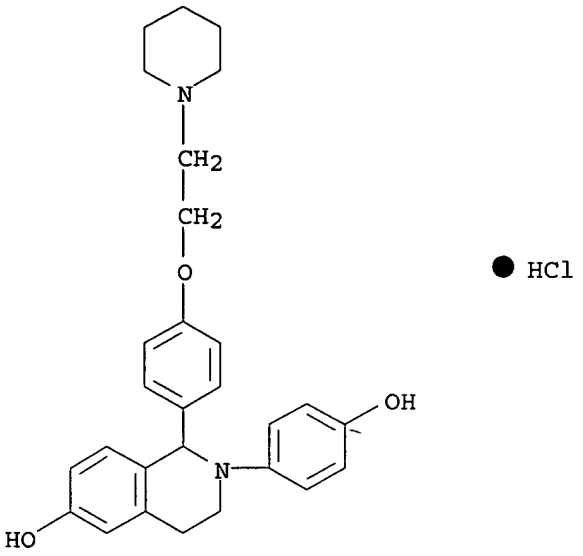


RN 180915-86-0 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-(4-hydroxyphenyl)-5-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (5R,6S)-rel- (9CI) (CA INDEX NAME)

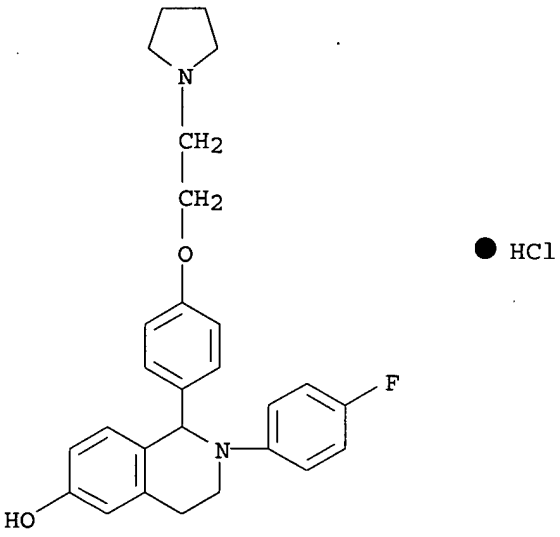
Relative stereochemistry.



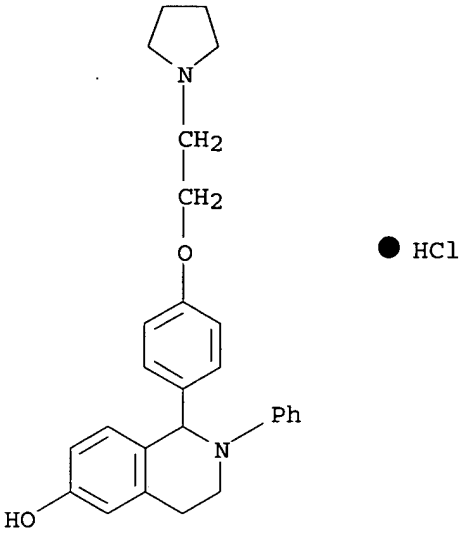
RN 180915-87-1 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)-1-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 180915-88-2 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

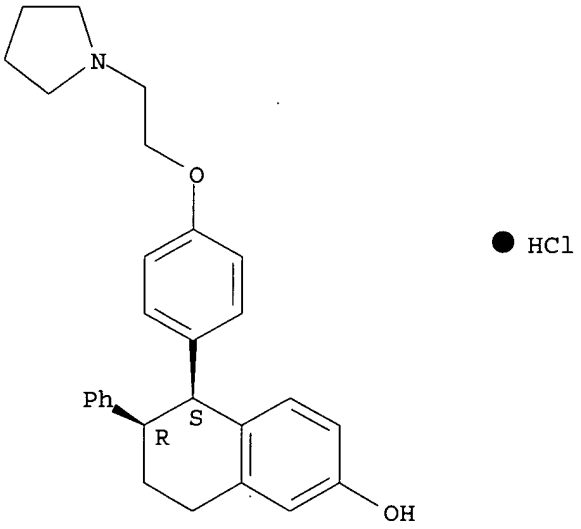


RN 180915-89-3 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



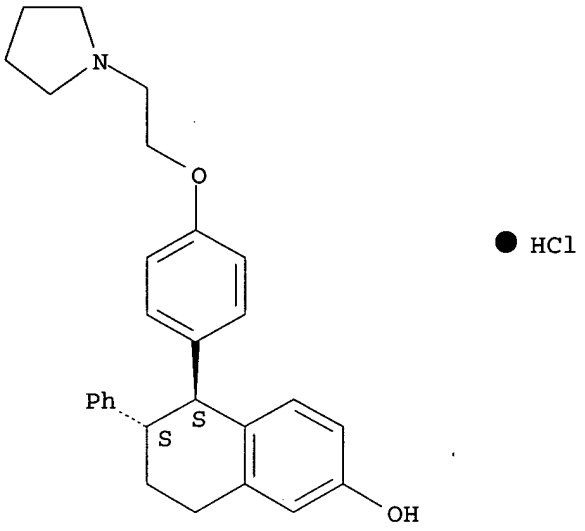
RN 180915-90-6 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, hydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



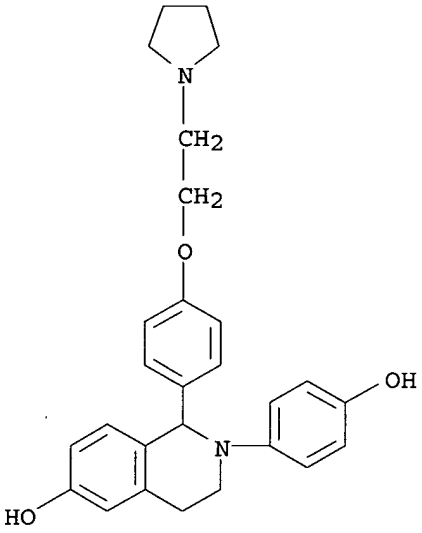
RN 180915-91-7 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, hydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



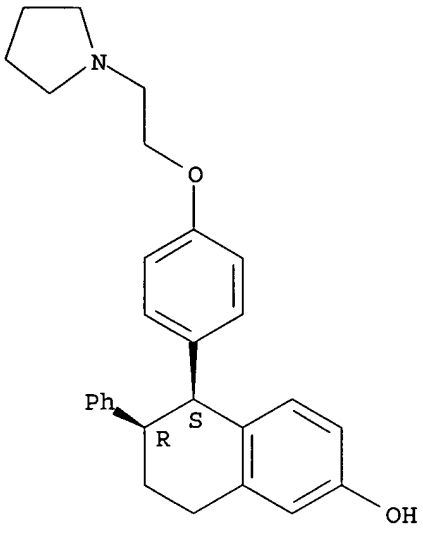
● HCl

RN 180915-92-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-(4-hydroxyphenyl)-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

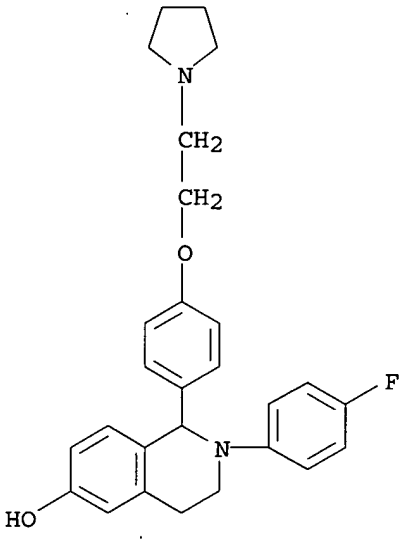


RN 180915-93-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5S,6R)- (9CI) (CA INDEX NAME)

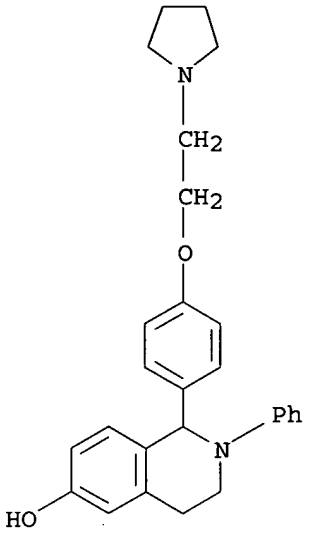
Absolute stereochemistry. Rotation (+).



RN 180916-14-7 HCAPLUS
CN 6-Isoquinolinol, 2-(4-fluorophenyl)-1,2,3,4-tetrahydro-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)

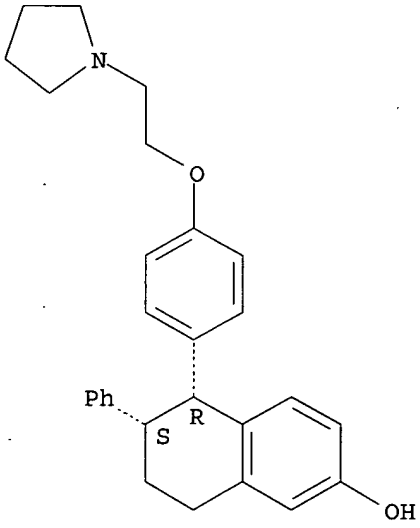


RN 180916-15-8 HCAPLUS
CN 6-Isoquinolinol, 1,2,3,4-tetrahydro-2-phenyl-1-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]- (9CI) (CA INDEX NAME)



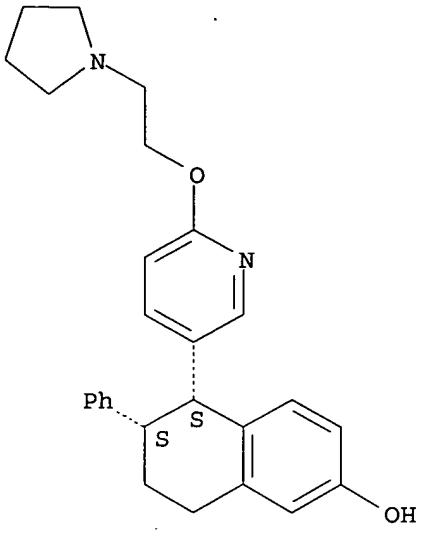
RN 180916-16-9 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 181137-16-6 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[6-[2-(1-pyrrolidinyl)ethoxy]-3-pyridinyl]-, (5S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

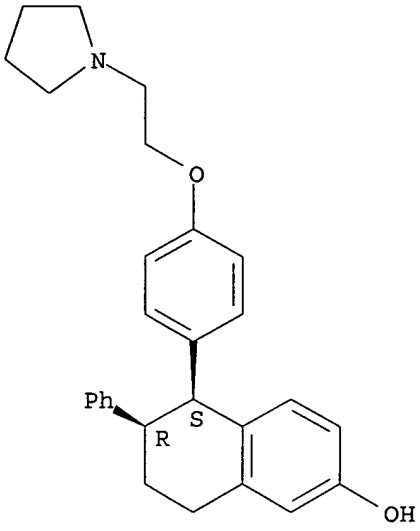


IT **180916-11-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 5-[4-(2-heterocyclylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ols and 1-[4-(2-heterocyclylethoxy)phenyl]-6-hydroxy-1,2,3,4-tetrahydroisoquinolines as estrogen agonists/antagonists)
RN 180916-11-4 HCAPLUS
CN 2-Naphthalenol, 5,6,7,8-tetrahydro-6-phenyl-5-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-, cis-, compd. with (R)-4-hydroxydinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin 4-oxide (1:1) (9CI) (CA INDEX NAME)

CM 1

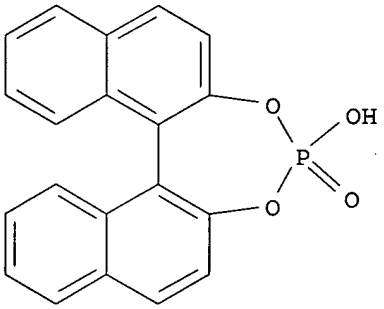
CRN 180915-78-0
CMF C28 H31 N O2

Relative stereochemistry.

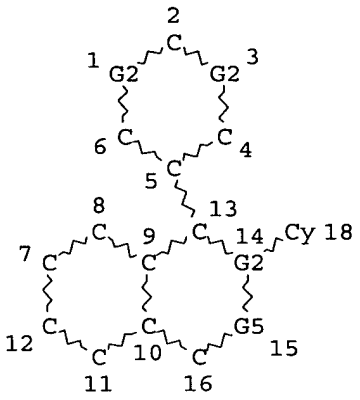


CM 2

CRN 39648-67-4
CMF C20 H13 O4 P



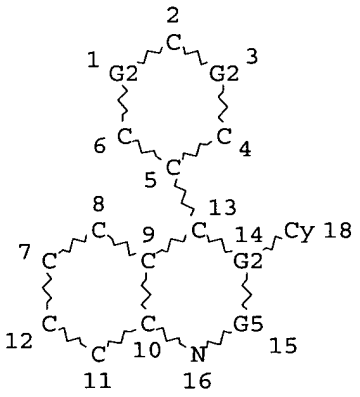
=> => d stat que l30
L7 SCR 1841
L14 STR



VAR G2=C/N
REP G5=(0-2) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

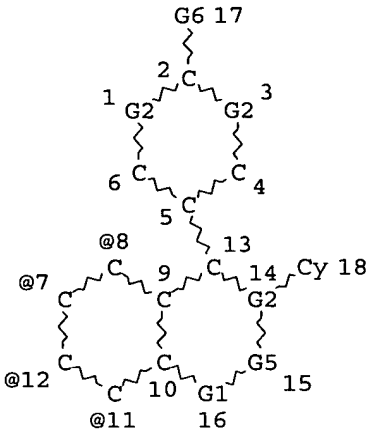
STEREO ATTRIBUTES: NONE
L16 STR



VAR G2=C/N
REP G5=(0-2) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L20 9814 SEA FILE=REGISTRY SSS FUL L14 OR L16 AND L7
L22 STR



N~G3 @19 20

C~G4~CH3 @21 22 23

O~C @24 25

S~C @26 27

OH @28

VAR G1=CH2/NH/19
VAR G2=CH/N
VAR G3=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/21
REP G4=(3-4) C
REP G5=(0-2) C
VAR G6=CH2/24/26
VPA 28-7/8/11/12 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE

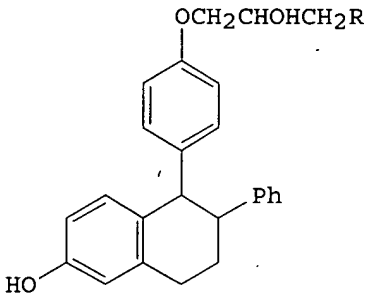
L23 87 SEA FILE=REGISTRY SUB=L20 SSS FUL L22
L24 130 SEA FILE=HCAPLUS ABB=ON PLU=ON L23
L25 33 SEA FILE=HCAPLUS ABB=ON PLU=ON L24(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARM?)
L26 58 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND (CARDIOVASCULAR DISEASE?/CV OR ATHEROSCLEROSIS?/CV OR HYPOGONADISM?/CV OR HYPERPLASIA?/CV OR OSTEOPOROSIS?/CV OR LIBIDO?/CV)
L27 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L24(L) (HEART(W)DISEASE OR ?ATHEROSCL? OR ?HYPOGONAD? OR ?HYPERPLA? OR ?OSTEOPOR? OR ?LIBID?)
L28 37 SEA FILE=HCAPLUS ABB=ON PLU=ON (L26 OR L27) NOT L25
L29 60 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 NOT (L25 OR L28)
L30 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND PD=<FEBRUARY 28, 1996

=>
=>

=> d ibib abs hitstr l30 1-8

L30 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:449032 HCAPLUS
DOCUMENT NUMBER: 115:49032
TITLE: Synthesis and biological behavior of a boronated analog of the antiestrogen U 23,469-M
AUTHOR(S): Wellmann, Folkert; Abraham, Ralph; Mueller, Rainer; Gabel, Detlef
CORPORATE SOURCE: Fachbereich Chem., Univ. Bremen, Bremen, D-2800/33, Germany
SOURCE: Zeitschrift fuer Naturforschung, C: Journal of Biosciences (**1991**), 46(3-4), 252-6
CODEN: ZNCBDA; ISSN: 0341-0382
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

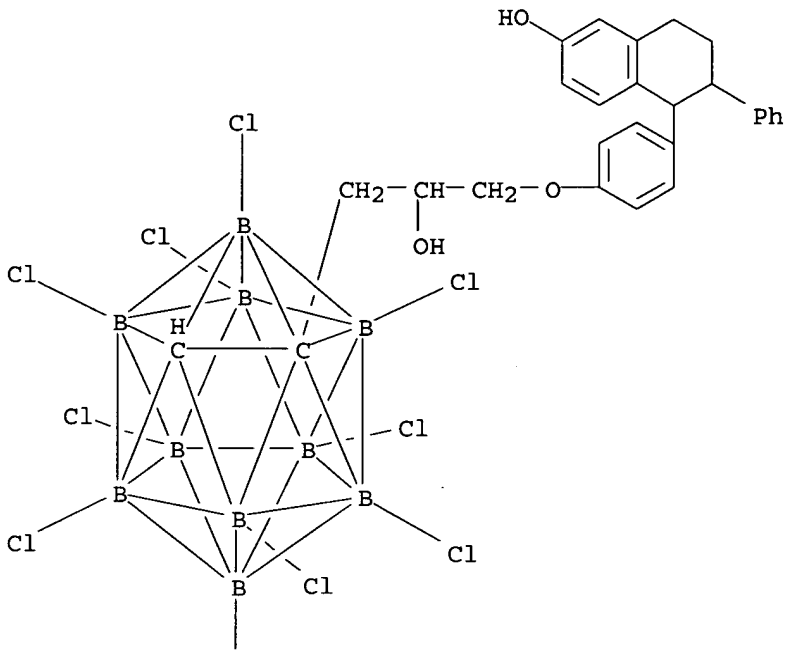
AB The title compound I (R = decachloro-o-carboranyl) was prepared, for possible use in neutron capture therapy of estrogen receptor-pos. tumors. This compound showed a large, non-specific uptake in ZR 75-1 breast cancer-derived cells. It partially inhibited the uptake of estradiol in these cells. Accumulation in the cells at physiol. obtainable concns. was, however, too low to envisage a therapeutic effect following thermal neutron irradiation

IT **98537-27-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and radio-sensitizing antitumor activity of)

RN 98537-27-0 HCAPLUS

CN 1,2-Dicarbadodecaborane(12)-1-ethanol, 3,4,5,6,7,8,9,10,11,12-decachloro-α-[[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L30 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:198542 HCAPLUS
DOCUMENT NUMBER: 108:198542
TITLE: Estrogen and antiestrogen interaction with estrogen receptor of MCF-7 cells - relationship between processing and estrogenicity
AUTHOR(S): Gyling, M.; Leclercq, G.
CORPORATE SOURCE: Institut Jules Bordet, l'Univ. Libre, Brussels, Belg.
SOURCE: Journal of Steroid Biochemistry (**1988**), 29(1), 1-8
CODEN: JSTBBK; ISSN: 0022-4731
DOCUMENT TYPE: Journal
LANGUAGE: English

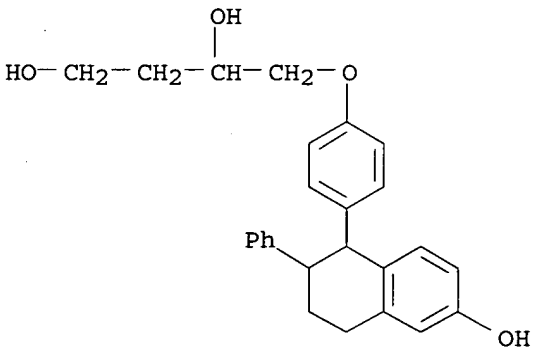
AB Overnight preincubation of MCF-7 cells with 2 + 10-10M estradiol (E2) produced a dramatic reduction of their specific [3H]E2 binding capacity. Scatchard plot anal. revealed that this loss of estrogen receptor (ER) concentration, usually termed processing, occurred without any modification of binding properties of the unprocessed receptors. Direct measurement of ER gave residual receptor concns. close to those established by binding assay, indicating that processing involved the loss of at least 1 epitope other than the steroid binding site. Incubation with increasing amts. of E2 (0.1 to 5 + 10-10M) resulted in an increasing reduction of binding capacity, indicating that the extent of processing was associated with the

hormone concentration Steroidal estrogens other than E2 as well as antiestrogens
of the triphenylethylene category behaved similarly in this regard, although the latter compds. usually acted only when at higher concns. The processing capacity of a large series of ligands was compared with the corresponding binding affinity for ER as assessed by classical competitive inhibition of [3H]E2 binding in both cytosol and whole cells. For steroidal estrogens, a large spectrum of concordant values was found which correlated with the known uterotropic activity of the compds. However, weak estrogen and antiestrogens of the triphenylethylene category displayed low processing capacities which were in the order of magnitude of the binding affinities established in whole cells; these values were considerably lower than the corresponding values measured in the cytosol. These observations are consistent with the concept that the capacity of a ligand to process ER is related to its agonistic activity. They also support the hypothesis (Stoessel, S.; Leclercq, G. 1986) that assessment of the ability of a ligand to inhibit the binding of [3H]E2 in whole cells provides an estimate of its agonistic activity, an estimate which can not be established in the corresponding cytosol assay.

IT **107144-85-4**
RL: BIOL (Biological study)
(estrogen receptor processing and mammary tumor cells response to, mol. structure in relation to)

RN 107144-85-4 HCAPLUS

CN 1,3-Butanediol, 4-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



L30 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1987:116021 HCAPLUS
DOCUMENT NUMBER:	106:116021
TITLE:	Competitive binding assay for estrogen receptor in monolayer culture: measure of receptor activation potency
AUTHOR(S):	Stoessel, S.; Leclercq, G.
CORPORATE SOURCE:	Clin. Lab. Cancerol. Mammaire, Univ. Libre Bruxelles, Brussels, 1000, Belg.
SOURCE:	Journal of Steroid Biochemistry (**1986**), 25(5A), 677-82 CODEN: JSTBBK; ISSN: 0022-4731
DOCUMENT TYPE:	Journal
LANGUAGE:	English

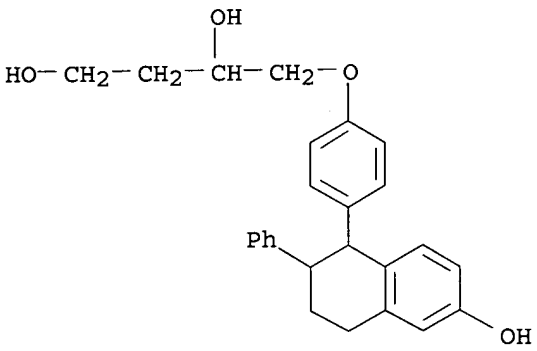
AB MCF-7 cells were incubated with [3H]estradiol, unlabeled estradiol, and various estrogens or antiestrogens to measure their relative binding affinity (whole-cell assay). Comparison of the values with those

previously established on uterine cytosol with a dextran-coated charcoal assay revealed a good parallelism for both steroid and diphenolic diethylstilbesterol based estrogens. On the contrary, in the whole-cell assay, antiestrogens and weak estrogens of the triphenyl- and gem-diphenylethylene categories always displayed low values which were in the order of magnitude found with weak steroid estrogens. This property was not due to a reduction of binding capacity, nor to the presence in some compds. of an ethoxy-aminoalkyl side-chain (source of antiestrogenicity). The present test can provide an estimate of the ability of a given compound to transform the receptor in a form which interacts with genomic sites involved in the regulation of estrogenic-induced products (activation).

IT **107144-85-4**
RL: ANST (Analytical study)
(estrogen receptors binding affinity for, of MCF-7 cells, receptor activation potency evaluation in relation to)

RN 107144-85-4 HCAPLUS

CN 1,3-Butanediol, 4-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



L30 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:97932 HCAPLUS

DOCUMENT NUMBER: 96:97932

TITLE: Effects of estrogens and antiestrogens on estrogen receptor dynamics and the induction of progesterone receptor in MCF-7 human breast cancer cells

AUTHOR(S): Eckert, Richard L.; Katzenellenbogen, Benita S.

CORPORATE SOURCE: Dep. Physiol. Biophys., Univ. Illinois, Urbana, IL, 61801, USA

SOURCE: Cancer Research (**1982**), 42(1), 139-44
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

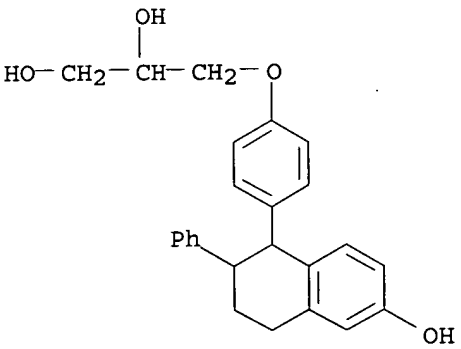
AB The effects of the estrogens estradiol [50-28-2] and diethylstilbestrol [56-53-1] and the triphenylethylene antiestrogens CI628 [5863-35-4], CI628M [76313-96-7], U23,469 [36840-93-4], and U23,469M [**72105-61-4**] on intracellular estrogen receptor (ER) dynamics and growth and progesterone [57-83-0] receptor induction were examined in MCF-7 human breast cancer cells. The relative binding affinities of the antiestrogens for cytoplasmic ER (ERC) were 1.0, 17, 0.04, and 34%, resp., in which the affinity of estradiol is considered 100%. Receptor-saturating concns. of CI628, CI628M, estradiol, and diethylstilbestrol (200, 10, 10, and 10 nM, resp.) caused complete ERC depletion and peak nuclear ER accumulation within 1 h. The nuclear receptor (ERN) sites declined thereafter and stabilized at near-control levels (1.2 pmol ERN/mg DNA) by

2-5 h, resulting in a net loss (processing) of approx. 50% of total cellular ER. In contrast, U23,469 (2000 nM) promoted complete depletion of ERC and quant. accumulation as ERN with 5 min, but the total ER content remained constant thereafter (no processing). U23,469M (60 nM) promoted complete ERC depletion and quant. nuclear accumulation, but the number of ERN sites subsequently declined slowly to reach the control level by Day 5. Among these compds., estradiol and diethylstilbestrol (0.1-1000 nM) promoted a 600% increase in cytoplasmic progesterone receptor (5 days, control = 0.2 pmol/mg DNA). CI628M and U23,469M (1-10 nM) produced only a 300% increase, and U23,469 and CI628 (0.1-1000 nM) did not promote any increase. ER translocation to the nucleus and progesterone receptor induction appear to be related to ligand affinity. Antiestrogens differ substantially from one another in their dynamics of interaction with ER and in their abilities to stimulate increases in cellular progesterone receptor. Processing of ER by antiestrogens such as CI628 does not ensure subsequent induction of progesterone receptor; and an apparently complex relation exists between the presence and duration of hormone receptor complexes in the nucleus and the induction of progesterone receptor in MCF-7 cells. Since all 4 antiestrogens inhibit MCF-7 cell growth but differ in their ability to increase cellular progesterone receptor levels, these studies indicate that growth and progesterone receptor induction are phenomena that are independently modulated by antiestrogens in these human breast cancer cells.

IT **72105-61-4**
RL: BIOL (Biological study)
(estrogen and progesterone receptors of cytoplasm and nucleus of human mammary cancer cells response to)

RN 72105-61-4 HCAPLUS

CN 1,2-Propanediol, 3-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



L30 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:202868 HCAPLUS

DOCUMENT NUMBER: 94:202868

TITLE: Antitumor activities and estrogen receptor interactions of the metabolites of the antiestrogens CI628 and U23,469 in the 7,12-dimethylbenz(a)anthracene-induced rat mammary tumor system

AUTHOR(S): Rorke, Ellen A.; Katzenellenbogen, Benita S.

CORPORATE SOURCE: Sch. Basic. Med. Sci., Univ. Illinois, Urbana, IL, 61801, USA

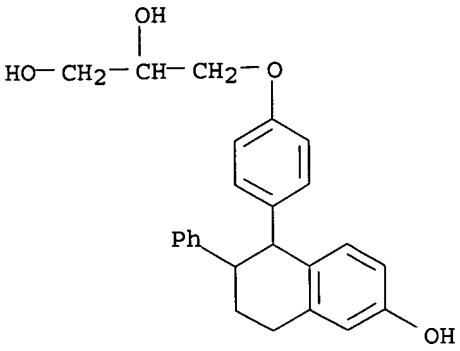
SOURCE: Cancer Research (**1981**), 41(4), 1257-62
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antitumor activities of the nonsteroidal antiestrogens α-{p-[2-(1-pyrrolidino)ethoxy]phenyl}-4-methoxy-α'-nitrostilbene (C1628) [10448-84-7] and cis-{3-[p-(1,2,3,4-tetrahydro-6-methoxy-2-phenyl-1-naphthyl)phenoxy]-1,2-propanediol} (U23,469) [36840-93-4] are compared with their demethylated metabolite forms in the dimethylbenz(a)anthracene-induced rat mammary tumor system. These demethylated forms are generated in vivo and are selectively accumulated in the nuclear estrogen receptor fraction in preference to the parent compound; thus, direct administration of the metabolites was investigated for eliciting tumor regression. The potencies of the parent antiestrogens and their demethylated forms α-{p-[2-(1-pyrrolidino)ethoxy]phenyl}-4-hydroxy-α'-nitrostilbene (CI628M) [76313-96-7] and cis-{3-[p-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthyl)-phenoxy]-1,2-propanediol} (U23,469M) [**72105-61-4**] were examined for stimulating the regression of established dimethylbenz(a)anthracene-induced mammary tumors. The effects of these antiestrogens on estrogen receptors and peroxidase [9003-99-0] as a sp. marker for estrogen action in mammary tumors and in uteri of tumor-bearing animals were also monitored. In mammary tumor cytosol in vitro, the antiestrogens completed with [3H]estradiol for binding to estrogen receptor with affinities of 113% (CI628M), 5% (CI628), 31% (U23,469M), and 0.6% (U23,469), where the affinity of estradiol is considered to be 100%. All 4 antiestrogens were equally effective as antagonists of tumor growth in vivo. Administration of 25 or 100 μg daily of either parent (CI628 and U23,469) or the demethylated (CI628M and U23,469M) antiestrogens elicited the regression of the majority of dimethylbenz(a)anthracene tumors, whereas low doses (2.5 μg/day) of any of these 4 compds. had no effect on tumor growth. The 25- and 100-μg doses of antiestrogens markedly reduced tumor cytoplasmic estrogen receptor levels, but they failed to elevate tumor peroxidase activity. Uterine wts. were decreased below the diestrus controls following treatment with 25- or 100-μg daily doses of the antiestrogens; these treatments also resulted in the nuclear localization of .apprx.80% of the total estrogen receptors. Uterine peroxidase activity, which was high in diestrus control females, was reduced to 5-25% by the intermediate- or high-dose levels of antiestrogens. Although the demethylated antiestrogens have a 20-50-fold enhanced affinity for the mammary tumor estrogen receptor in vitro as compared to their parent compound in vivo, where the parent compds. are rapidly converted to the demethylated metabolites, both forms are equally potent antitumor and antiuterotropic agents.

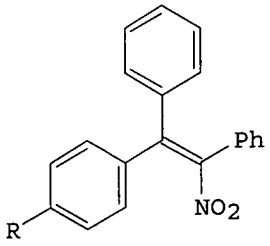
IT **72105-61-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm-inhibiting activity of, estrogen receptor interactions in relation to)

RN 72105-61-4 HCAPLUS
CN 1,2-Propanediol, 3-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)

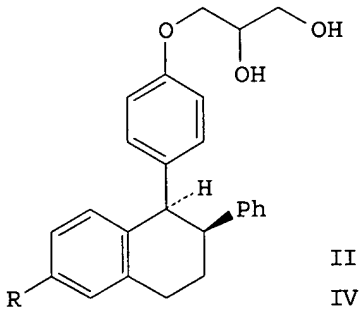


L30 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:96523 HCAPLUS
DOCUMENT NUMBER: 94:96523
TITLE: Biological potency and uterine estrogen receptor interactions of the metabolites of the antiestrogens CI628 and U23,469
AUTHOR(S): Hayes, James R.; Rorke, Ellen A.; Robertson, David W.; Katzenellenbogen, Benita S.; Katzenellenbogen, John A.
CORPORATE SOURCE: Coll. Med., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Endocrinology (**1981**), 108(1), 164-72
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=OMe
III, R=OH



II, R=OMe
IV, R=OH

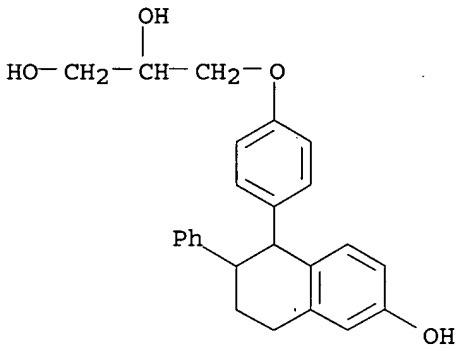
AB Two potent nonsteroidal antiestrogens, CI682 (I) [5863-35-4] and U 23469 (II) [36840-93-4] and the demethylated metabolite forms of the parent antiestrogens, CI628M (III) [76313-96-7] and U23,469M (IV) [**72105-61-4**] were compared with regard to potency in terms of their (1) affinity for cytoplasmic estrogen receptor, (2) ability to translocate estrogen receptor to the nuclear fraction in whole uteri in organ culture in vitro and to prevent nuclear uptake of 3H-labeled estradiol [50-28-2], (3) ability to prevent estradiol stimulation of induced protein synthesis in vitro, and (4) ability to inhibit estradiol stimulation of uterine weight gain and peroxidase [9003-99-0] activity in vivo. The antiestrogens compete with [3H]estradiol for binding to cytosol estrogen receptor with the following affinities: III, 135%; IV, 30%; I, 11%; and II, 0.1%, where estradiol affinity is considered 100%. In whole uteri in vitro, all 4 compds. deplete cytoplasmic receptor and translocate estrogen receptor

into the nucleus, and they prevent nuclear localization of [3H]estradiol and inhibit estradiol stimulation of induced protein synthesis in a dose-related fashion; III and IV are more potent, being as effective as their parent compds. at 10-100-fold lower doses. In 3-day in vivo assays, dose-response curves indicate that the metabolites and parent compds. are equally potent in inhibiting estradiol-stimulating uterine weight gain and peroxidase activity. Thus, the demethylated metabolites of the antiestrogens have a higher affinity for receptor and a greater biol. potency in vitro. However, in vivo, where the parent compds. are rapidly and efficiently converted to the metabolites, both forms have comparable potencies.

IT **72105-61-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiestrogenic activity of)

RN 72105-61-4 HCAPLUS

CN 1,2-Propanediol, 3-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



L30 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:41585 HCAPLUS

DOCUMENT NUMBER: 94:41585

TITLE: Antiestrogen action in estrogen target tissues: receptor interactions and antiestrogen metabolism

AUTHOR(S): Katzenellenbogen, Benita S.; Katzenellenbogen, John A.; Eckert, Richard L.; Hayes, James R.; Robertson, David W.; Tatee, Tochiro; Tsai, Ten-lin S.

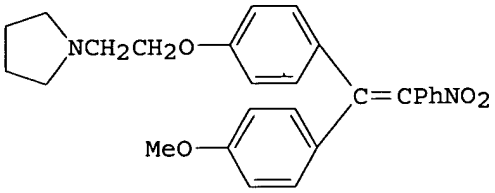
CORPORATE SOURCE: Dep. Physiol., Univ. Illinois, Urbana, IL, 61801, USA

SOURCE: Progress in Cancer Research and Therapy (**1980**), 14(Horm. Cancer), 309-20
CODEN: PCRTDK; ISSN: 0145-3726

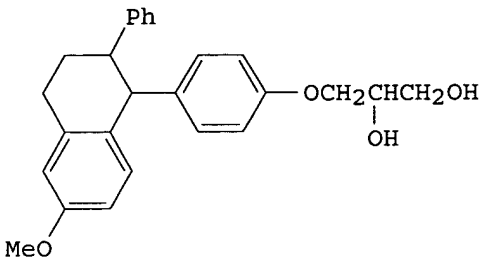
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



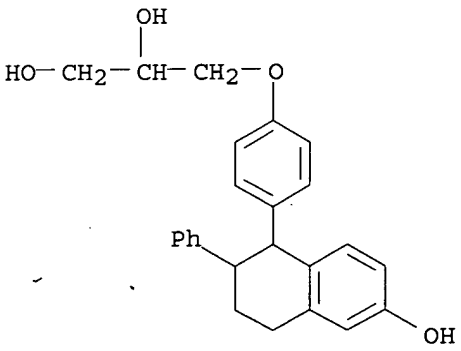
II

AB Uterine nuclear receptor antiestrogen complexes from rats injected with CI-628 (I citrate) [5863-35-4] sedimented in sucrose d. gradients in a similar manner to the receptor complex of rats treated with estradiol [50-28-2]. Nuclear antiestrogen- and estradiol-receptor complexes from DMBA-induced mammary tumors were also indistinguishable by sucrose d. gradient anal. The demethylated metabolites of I and U-23469 (II) [22845-61-0] had a much higher binding affinity for estrogen receptors in rat uterine cytosol and for nuclear or cytosol receptors in MCF-7 human breast cancer cells than did their resp. parent compds. Apparently, I and II are metabolized to compds. with a higher affinity for receptor and a faster onset of action. A discussion is included on the mol. aspects of the mode of action of antiestrogens.

IT **72105-61-4**
RL: PROC (Process)
(estrogen receptor binding of, in mammary tumors and uterus)

RN 72105-61-4 HCAPLUS

CN 1,2-Propanediol, 3-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



L30 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:16102 HCAPLUS
DOCUMENT NUMBER: 92:16102
TITLE: Antiestrogens and antiestrogen metabolites:

preparation of tritium-labeled (±)-cis-3-[p-(1,2,3,4-tetrahydro-6-methoxy-2-phenyl-1-naphthyl)phenoxy]-1,2-propanediol and characterization and synthesis of a biologically important metabolite

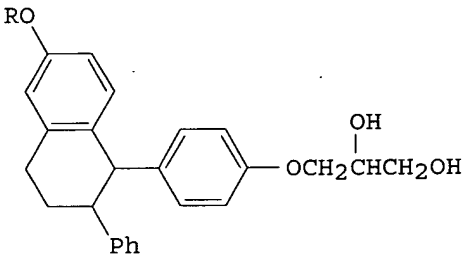
AUTHOR(S): Tatee, Tochiro; Carlson, Kathryn E.; Katzenellenbogen, John A.; Robertson, David W.; Katzenellenbogen, Benita S.

CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA

SOURCE: Journal of Medicinal Chemistry (**1979**), 22(12), 1509-17
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 92:16102

GI



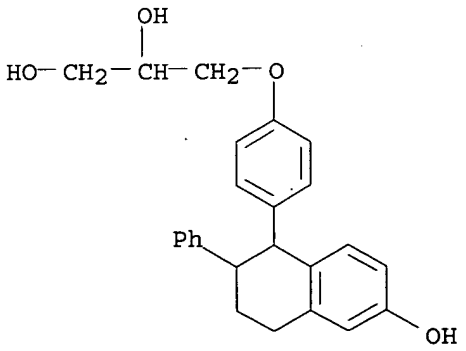
I, R=Me
II, R=H

AB The 3H-labeled title compound I [72105-60-3] was prepared by alkylation of 3H-labeled cis-1-(p-hydroxyphenyl)-2-phenyl-6-methoxy-1,2,3,4-tetrahydronaphthalene [72105-59-0] with 3-iodo-1,2-propanediol [554-10-9]. In in vivo studies in immature rats I was converted to 1-[p-(2,3-dihydroxypropoxy)phenyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydronaphthalene (II) [**72105-61-4**], a more polar metabolite that accumulated selectively in estrogen receptor sites in uterine nuclei. The receptor binding affinity of II was ≥300-fold greater than that of I.

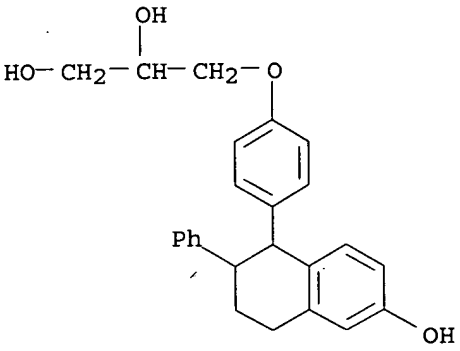
IT **72105-61-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antiestrogen activity of)

RN 72105-61-4 HCAPLUS

CN 1,2-Propanediol, 3-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]- (9CI) (CA INDEX NAME)



IT **72105-65-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by microsomal demethylation)
RN 72105-65-8 HCAPLUS
CN 1,2-Propanediol, 3-[4-(1,2,3,4-tetrahydro-6-hydroxy-2-phenyl-1-naphthalenyl)phenoxy]-, labeled with tritium (9CI) (CA INDEX NAME)



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